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THE DIAGNOSTIC VALUE OF ARTERIOGRAPHY OF THE ILIAC ARTERY IN GYNAECOLOGY AND OBSTETRICS

by

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Medical literature contains few references to the subject of arteriography of the human uterine artery in vivo. SAITO and KAMIKAWA (1930) described a method for the roentgen examination of the blood vessels of the pelvis; they exposed the femoral artery and a retrograde injection of an opaque medium was made into the blood stream. However, they did not mention whether they also succeeded in filling the uterine artery by this method. SAITO (quoted from ITOH, 1939) reported that he successfully filled the uterine artery at aortography in two cases. FARIÑAS (1946) studied the abdominal aorta and the iliac artery using the same method as SAITO and KAMIKAWA. He did not mention filling of the uterine artery in the article but published a radiograph of a myoma in which this vessel was visible.

HARNETT (1948) made aortographic studies in pregnant women and succeeded in filling the uterine artery. He could thus determine the point of attachment of the placenta, and in two cases he was able to establish the diagnosis of placenta praevia. He published radiographs showing the placental sinuses in normal cases and in cases of placenta praevia. However, a few accidents have occurred with aortography. Moreover, the examination has to be conducted under general anaesthesia. It has also been reported that it may induce labour in women near term (HARNETT, 1948).

The above review of the literature shows that up to now percutaneous retrograde arteriography has not been used either for the differential diagnosis of gynaecological lesions in the pelvis or for the determination of the site of the placenta.

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There is every indication, however, that visualization of the uterine artery could be used as a guide to the differential diagnosis of tumours in the pelvis. In the first place it would aid in distinguishing ovarian tumours from growths arising from the uterine wall, because the uterus and the ovaries derive most of their blood supply from different sources. Admittedly, a differential diagnosis of these tumours can usually be made at the vaginal examination by bimanual palpation. Still, there are cases in which it fails to give the desired information.

This paper sets out to consider the diagnostic value of visualization of the uterine artery by percutaneous retrograde arteriography of the iliac artery in doubtful cases. In many cases of this series arteriography was combined with hysterosalpingography, which made it possible to assess the thickness of the uterine wall, thus contributing additional diagnostic information. These investigations have been in progress since 1949.

Technique

The course of the femoral artery in the region of the inguinal ligament was outlined, and local anaesthesia was induced by infiltration with novocain. A tourniquet was placed on the femoral artery below the inguinal ligament above the origin of the deep femoral artery (Fig. 1). The compression should be sufficient to arrest the circulation. The needle used for puncturing the artery was introduced immediately above the tourniquet. After having perforated the artery the needle was turned upwards and pushed right into the lumen and then 3 to 5 cm. along the external artery. A blunt stilet was then introduced into the needle to arrest the bleeding. After having verified that the compression was adequate, arteriography was carried out. In cases in which hysterosalpingography was also called for, the opaque me-

Fig. 1. Patient ready for arteriography. Tourniquet on the femoral artery below the inguinal ligament above the origin of the deep femoral artery.

dium used for this procedure, was injected before performing arteriography.

In the initial stages of this investigation a 35 per cent solution of umbradil (perabrodil) was used as the opaque medium for arteriography. Later, it was replaced by an opaque medium deviced by BACKMAN (1951) which is more viscous and consists of one part of a 22 per cent solution of dextran (macrodex) and two parts of a 50 per cent solution of umbradil. As a rule, the opaque medium was injected in 3 to 4 seconds. The first exposure was made towards the end of the injection of the opaque medium. A further two exposures were taken 2 to 5 seconds after the first.

In cases in which an insufficient amount of the opaque medium passed through the aorta into the iliac artery on the opposite side, it was often also necessary to investigate that side.

Cases Studied

101 cases in all were studied. In the initial stages of this investigation unsatisfactory results were often obtained because of extravasation of the opaque medium or because filling was incomplete. In 70 cases a satisfactory filling of the uterine artery was obtained, and a fair interpretation of the arteriograms was possible. 57 of these 70 cases were later operated upon. With increasing skill, however, the number of radiographs, in which the uterine artery could be visualized, also increased, and it hardly ever happens now that the uterine artery does not show up well.

The Normal Arteriogram

Several authors have studied the course of the uterine artery in the normal uterus. These studies, made on operative or autopsy material, have shown that the course of the uterine artery follows a typical and uniform pattern in the normal uterus. This observation was confirmed in this investigation.

As already mentioned, three exposures were usually made. Fig. 2 a shows the first radiograph in a normal case. As may be seen, the opaque medium fills the external iliac artery as far as the division of the aorta. In many cases filling of the iliac arteries on the opposite side was also obtained. Fig. 2 a shows that the uterine artery arises from the internal iliac artery immediately above the point of origin of the superior gluteal artery; it runs first over the lateral wall of the true pelvis, and then runs medially towards the cervix. Immediately before it reaches the uterus

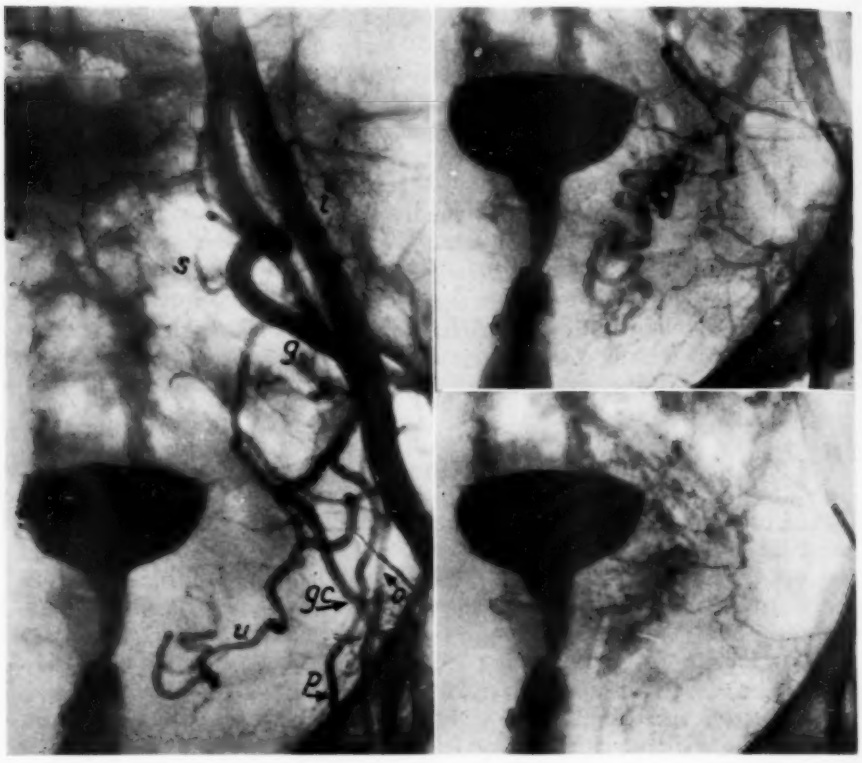


Fig. 2. Arteriogram and hysterogram in a normal case. *a*. Towards the end of the injection. Uterine artery (u) filled as far as uterus; intramural vessels not visible. Other arteries: i, external iliac; s, lateral sacral; g, superior gluteal; o, obturator; g. c. inferior gluteal; p, pudendal. *b*. 2 seconds later. Uterine artery and intramural vessels filled. *c*. 2 seconds after exposure *b*. Uterine artery no longer visible; intramural vessels filled.

it gives off a vaginal branch. At the level of the cervix it changes its course and ascends upward along the lateral margin of the uterus as far as the fundus, following a more or less tortuous course.

In Fig. 2 b, which shows the second arteriogram, it may be seen that the uterine artery is filled with the opaque medium, and that the fine blood vessels in the uterine wall all have the typical corkscrew appearance and show up well. In some cases a few fine vessels, often tortuous and running laterally towards the adnexa, could also be seen in the second arteriogram (Fig. 3).

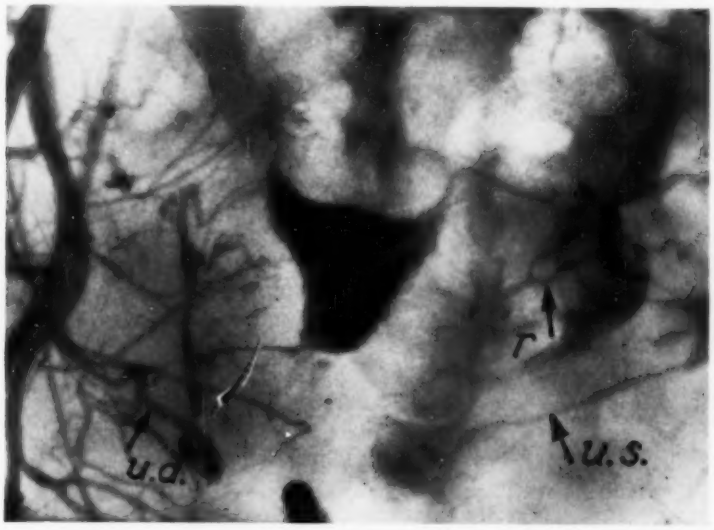


Fig. 3. Arteriogram and hysterosalpingogram in normal case. The right artery (u. d.) follows a straight course over the lateral wall of the uterus; that on the opposite side is faintly visible but branches running towards the adnexa (r) show up well.

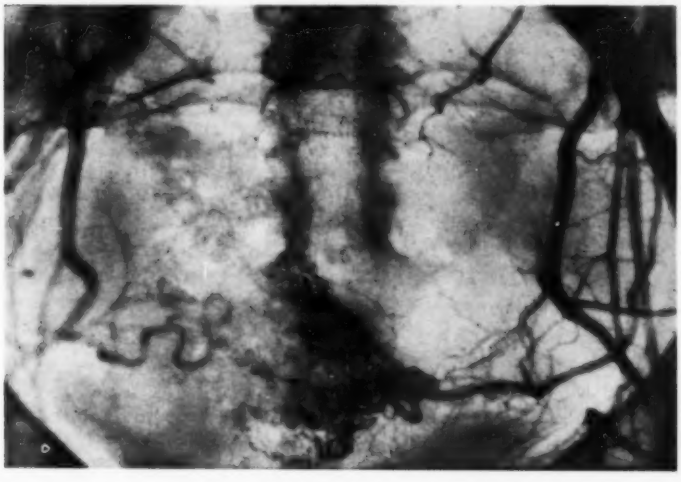


Fig. 4. Arteriogram in case of leftsided ovarian cyst. Uterine artery displaced downwards (cf. the normal uterine artery on the opposite side).

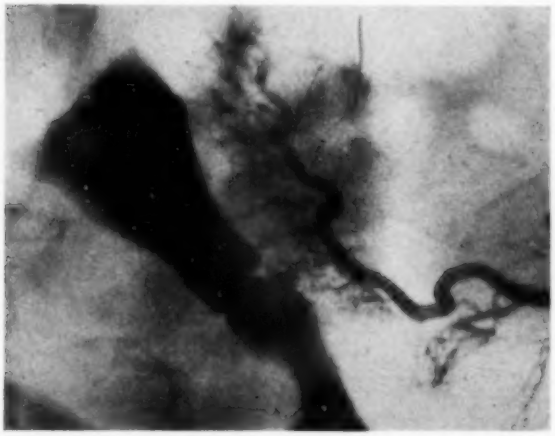


Fig. 5. Leftsided ovarian cyst. Arteriogram and hysterosalpingogram. The uterus is displaced to the right and retroflexed. The uterine artery is normal.

Fig. 2 c shows the third arteriogram in which the uterine artery is no longer visible. Further, it may be seen that the finest intramural vessels are incompletely filled.

The vascular pattern in the normal uterus naturally varies according to the position of the uterus. If it be markedly anteflexed and anteverted the direction of the central ray runs parallel with the long axis of the main branch of the uterine artery but the finer vessels in the myometrium show up well (Fig. 4). If the uterus be retroflexed and retroverted it is possible to follow the course of the uterine artery within quite a large area in the arteriogram (Figs. 3 and 5).

Although the number of normal uteri studied was relatively small the observations made on some arteriograms suggested that in nulliparae (Fig. 3) the uterine artery follows a straighter course as it passes along the lateral margin of the uterus than in multiparae, in whom it is more or less tortuous.

It was also observed that the number of intramural vessels which could be filled varied during the phases of the menstrual cycle; *e. g.*, shortly before an expected menstruation a larger number of intramural vessels were visible. The blood supply of the uterus before and after the injection of oestradiol benzoate was also investigated in patients suffering from secondary amenorrhoea of long standing; it was found that it increased markedly following this treatment (Fig. 6). These problems will be the subject of particularized research.

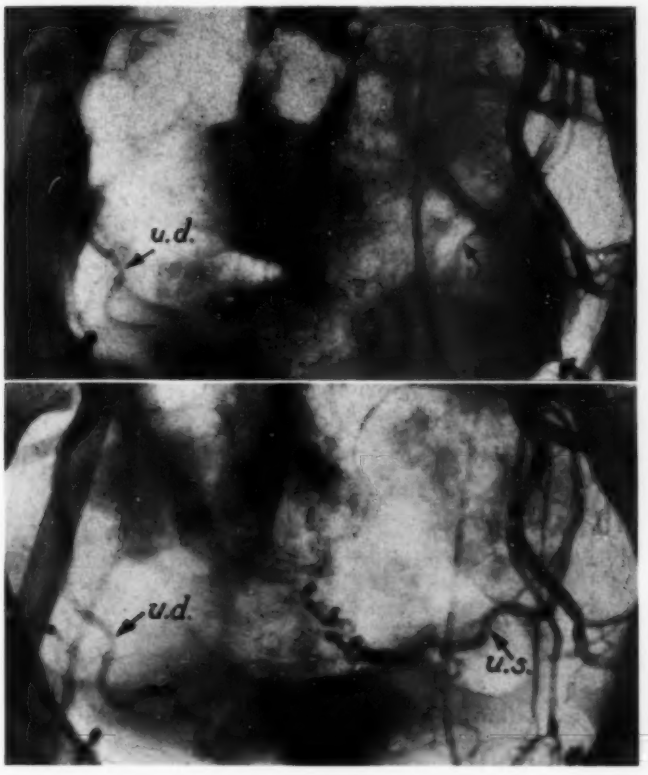
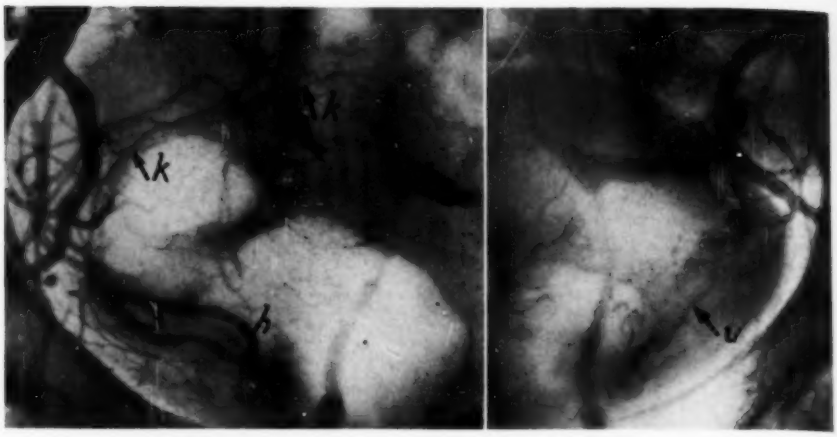


Fig. 6. Arteriogram in a case of secondary amenorrhoea. Past history: Bilateral oophorectomy. *a*. Before treatment with oestradiol benzonate. The vessels in the true pelvis show up well except the uterine arteries which are only faintly visible. *b*. After intramuscular administration of 200,000 IbU of oestradiol benzoate. The exposure was made about the same time as exposure *a*, u. d., right uterine artery; u. s., left uterine artery.

The Arteriogram of the Uterine Blood Vessels in Gynaecological Disease

Ovarian Tumours. This series included 12 cases of ovarian tumour. With the exception of one, all these patients were treated surgically and the diagnosis was verified at operation. If the growth caused a marked displacement of the uterus and a stretching of the parametrium. the course of that portion of the uterine artery which runs through the



a. b.

Fig. 7. Arteriogram and hysterogram in case of intramural myoma on the right side. *a*. Right uterine artery is widened. At the level of the cervix it forms a 'hair-pin bend' (h). Branches are seen in the capsule of the myoma (k). *b*. Left uterine artery (u) is normal. The myoma is supplied by the uterine artery on the right side only.

parametrium was almost straight (Fig. 4). Changes in the width of the uterine artery or its course within the uterus were not observed (Fig. 5); nor was there any evidence of changes in the branches which run towards the adnexa.

Uterine Myomata. SAMPSON (1912), BARDON (1921), HOLMGREN (1938), FAULKNER (1944), and others studied the blood vessels in uteri containing myomata in specimens removed at operation. These authors demonstrated that the vascular picture was quite unlike the normal one, an observation which was confirmed in this investigation.

This series included 33 cases of uterine myomata; in 20 of them the patient was operated upon. Arteriography revealed the following characteristic features:

1. In all cases, in which the myoma was the size of a man's closed fist or larger, the uterine artery was widened. If the myoma was smaller the uterine artery was either widened or normal in width. If the growth was very small, *e. g.* the size of a hazelnut or walnut, there was no evidence of an increase in width. The latter observation agrees closely with those made by earlier workers; *e. g.*, SAMPSON (1912) and others observed that, with the exception of very small myomata, the arterial vascularity of the growths is generally extensive. It is reasonable to assume that as the arterial vascularity increases the uterine artery also becomes wider.

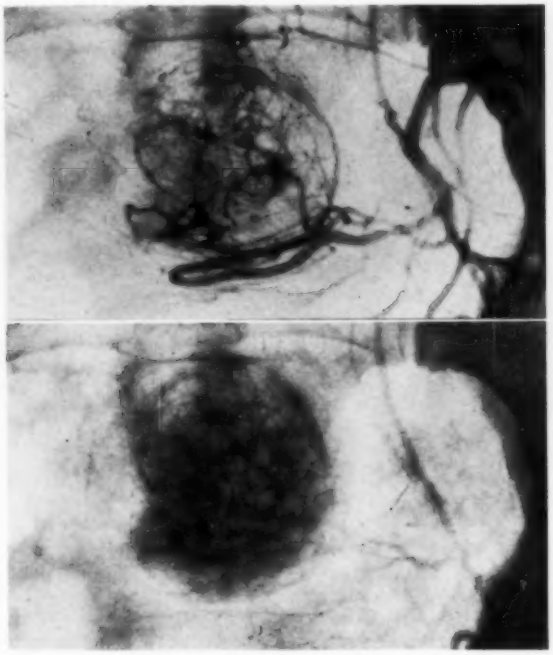
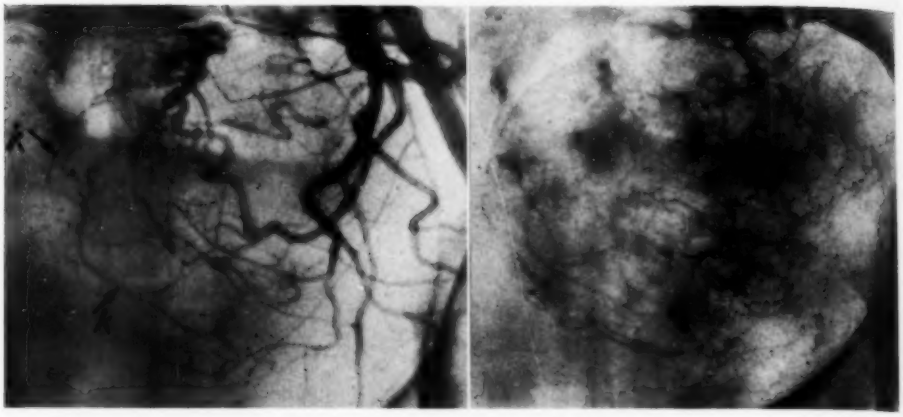


Fig. 8. Arteriogram in case of a myoma in the corpus on the left side. *a*. The left uterine artery is slightly widened and forms a 'hair-pin bend'. Capsular and 'intrinsic arteries' show up. *b*. 2 seconds after exposure *a*. 'Intrinsic arteries' are visible except in the right pole of the myoma, probably because this portion is supplied by the right uterine artery.

2. Myomata situated in the lower part of the uterus near the cervix displaced the ascending portion of the uterine artery laterally; the vessel followed a course the pattern of which could be likened to a 'hair-pin bend' (Figs. 7 a, and 8 a).

3. It was found that myomata are nourished by the intramural arteries. Before they penetrated the substance of the growth they were often seen in the form of straight and slightly curved vessels which surrounded the myoma and lacked the normal corkscrew appearance. In a few cases the presence of these vessels enabled us to diagnose myomata the size of hazelnuts (Figs. 7 a, 8 a, 9 a, and 11).

4. The arteries in small myomata were often scanty. As a rule, it was not possible to identify any arteries at all either in the periphery



a. b.

Fig. 9. Arteriogram in a case of pedunculated myoma the size of a man's closed fist. *a*. The uterine artery is slightly widened. Vessels (k) are visible in the capsule of the growth. *b*. About 2 seconds after exposure *a*. A large number of 'intrinsic vessels' are visible.

or in the substance of the growths. Nevertheless, the abnormal course of the intramural arteries caused by the tumours led to their diagnosis.

5. As already mentioned, the arteries in the large myomata were often numerous. Typical 'intrinsic arteries' (SAMPSON, 1912) showed up in the substance of the tumours. The appearance of these vessels deviated from that of the normal uterine blood vessels; they followed a rather abnormal course, which tended to be straighter than that followed by the normal uterine blood vessels, and communicated with one another and gave off branches; the vascular pattern could be likened to a tree or a bush. They usually showed up well in the arteriogram (Figs. 8 a, b, and 9 b).

6. Arteriography combined with hystero-salpingography made it possible to determine the thickness of the wall of the corpus uteri. In the presence of myomata there was often a diffuse thickening of the wall. A localized thickening was observed only in a few cases. The possibility of determining the site of a myoma in relation to the Fallopian tubes is naturally of great clinical importance.

The distribution of these features among the 33 cases of this series was as follows: Vessels in the capsule of the tumour, 20 cases; a widened uterine artery, 15 cases; a typical 'hair-pin bend' of the uterine artery, 11 cases; 'intrinsic vessels', 10 cases; distorted intramural vessels, 1 case.

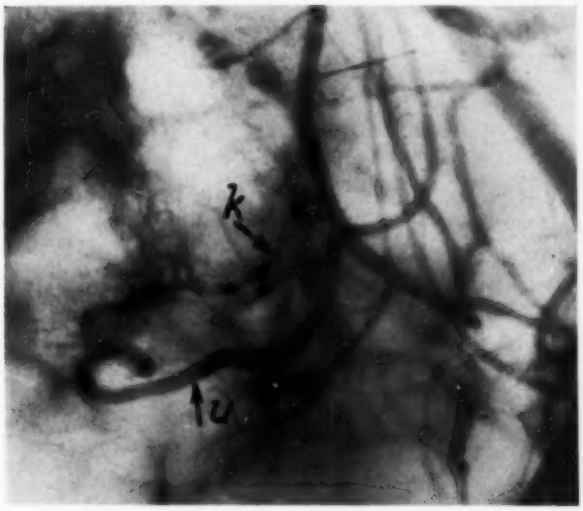


Fig. 10. Arteriogram in a case of myoma the size of a walnut involving the left uterine horn. The uterine artery (u) follows a normal course as far as the fundus where it gives off a small branch (k) in the capsule of the growth.

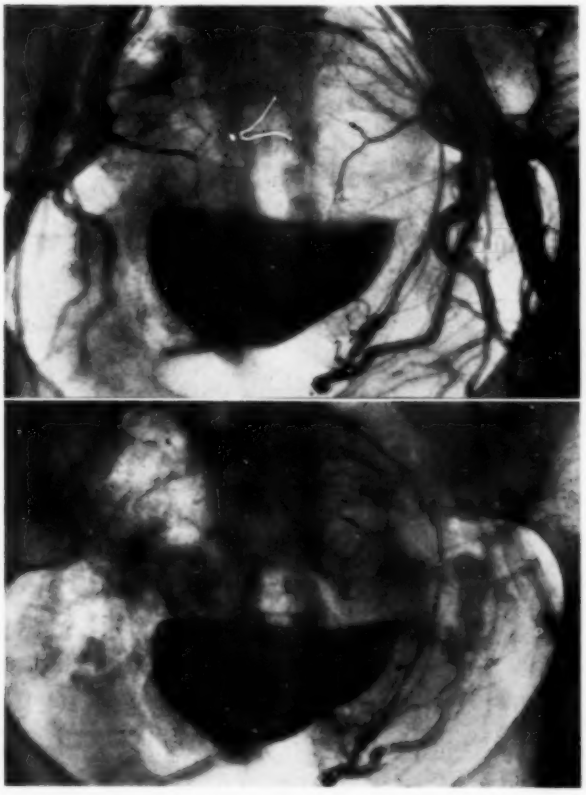
In some cases the myomata were supplied by the uterine artery of one side only (Figs. 7 a and b). If the uterine artery of one side is found to be normal that of the opposite side should also be investigated; otherwise, the possibility of a myoma being present cannot be excluded with certainty. In 6 cases we failed to establish the correct diagnosis probably because the uterine artery of one side only was examined.

In 2 cases the arteriogram revealed a calcareous myoma. In one of these cases the blood vessels did not show the features typical in a myomatous uterus; in the other a widened uterine artery was the only abnormality found.

Arteriographic Studies during Pregnancy

In 21 cases arteriography was carried out during pregnancy; in 12, this examination was made before the 5th month, and in 2 in the last months of pregnancy.

It could not be definitely established whether the width of the uterine artery began to increase as early as in the 1st month of pregnancy, but in the 2nd month there was evidence that it had increased (Figs. 12 b and 13 a). The radiographs taken during the following months revealed

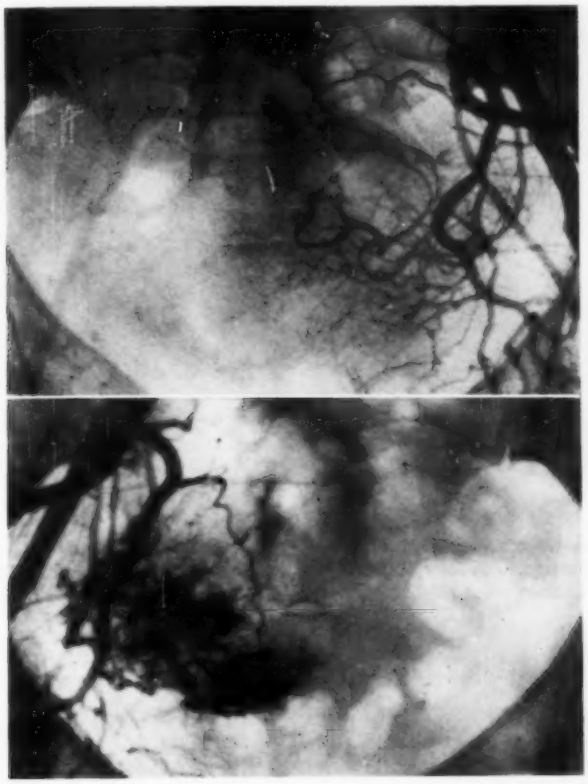


a.

b.

Fig. 11 a—b. Arteriogram and hysterogram in a case of myoma the size of a tennis ball situated in the fundus. The course of the uterine artery as it runs on along the uterus to the fundus is straight.

that it continued to increase. It was found that, as the vessel widened, it became less tortuous. In the last month of pregnancy its course over the uterine wall was quite straight. It was also observed that immediately before the uterine artery ran into the placental sinuses it gave off a large number of branches which all were slender and very tortuous. The placental sinuses were clearly visible from the 3rd month of pregnancy onwards which made it possible to determine the site of the placenta. As a rule, the placental sinuses filled readily and were still visible in the third arteriogram.



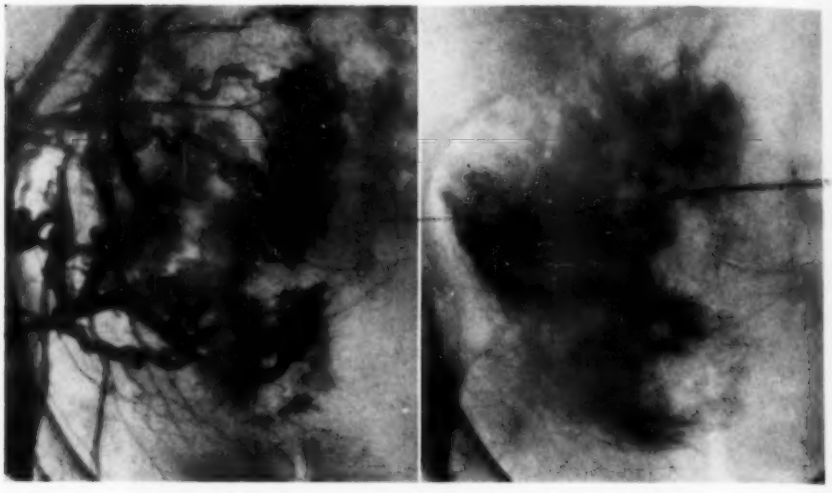
a.

b.

Fig. 12. Arteriogram in the 2nd month of a normal pregnancy. *a*. Left uterine artery. Filling of the placental sinuses was not obtained from this side. *b*. Right uterine artery. The placental sinuses are visible. Both uterine arteries are wider and their distribution larger than normal.

The 'hair-pin bend' of the uterine artery, which is typical of a uterus containing myomata, was also observed during pregnancy. This pattern is produced by the enlargement of the corpus uteri which causes a lateral displacement of the uterine artery.

Hence, a 'hair-pin bend' of the uterine artery and an increase in its width was observed during pregnancy as well as in a uterus containing a myoma. It is, however, possible to distinguish an early pregnancy from a myoma because 'intrinsic arteries' are not seen during pregnancy,



a. b.

Fig. 13. Arteriogram in the 4th month of a normal pregnancy. *a*. Exposure towards the end of injection. The uterine artery is markedly widened but still tortuous. *b*. 2 seconds after exposure *a*. The placental sinuses are visible.

and vessels resembling placental sinuses are absent in a myomatous uterus.

In a few cases the placenta was supplied by the uterine artery of one side only (Figs. 12 a and b). The films generally suggested that some of the placental sinuses were fed by the uterine artery of one side while the remainder were supplied by that of the opposite side. The site and the size of the placental sinuses cannot be accurately determined unless the uterine arteries of both sides are investigated. In one case of placenta praevia we failed to diagnose the condition, probably because only one uterine artery was examined.

Arteriographic Studies during Extra-uterine Pregnancy.

Arteriography has hitherto been carried out only in one case of extra-uterine pregnancy. It was found that the tubal branch showed up very well and that its width corresponded to that of the main branch of the uterine artery (Fig. 14 a). The opaque medium was seen in the form of three small spots in the lateral upper corner of the true pelvis within an area twice the size of the tip of a thumb (Fig. 14 b). These spots, the outlines

a. b.

Fig. 14. Arteriogram in case of tubal pregnancy. *a*. The tubal branch (r) is widened. *b*. Small placental sinuses (arrow) are filled in the lateral upper corner of the true pelvis.

of which were very irregular, represented placental sinuses. The irregular outlines were caused by villi and septa.

It is likely that an extra-uterine pregnancy produces typical arteriographic appearances which may be of great diagnostic value. It is hoped that the studies in progress will contribute to the clarification of these problems.

Discussion

The investigation has shown that practically all myomata cause typical changes in the appearance of the uterine blood vessels. Arteriography, therefore, is of diagnostic value in cases in which it is not possible to make a definite diagnosis by vaginal examination. In cases, in which a myoma coexists with an ovarian tumour, the correct diagnosis may present difficulties. If, however, the arteries of both sides are examined it is possible to obtain an idea of the size of the myoma as well as of conditions in general. If, in such cases, palpation reveals a mass, larger than that disclosed by bilateral arteriography, there are good reasons to suspect that an extra-uterine tumour co-exists.

In some cases it was possible to determine the thickness of the uterine wall by combining arteriography with hystero-salpingography, which

contributed additional diagnostic information. In some cases the abnormal course of the portion of the uterine artery which extends through the parametrium, enabled us to diagnose an adnexal tumour. However, it was not possible to determine whether the displacement was caused by a tumour arising from the Fallopian tubes or by one arising from the ovary. In such cases the correct diagnosis depends on a critical study of the other clinical features.

The number of cases in which arteriography was carried out during pregnancy, was relatively small. Nevertheless, the observations made on the pregnant uterus indicated that the site of the placenta can be determined by percutaneous retrograde arteriography of the iliac artery. The examination, therefore, seems to be a valuable aid in the diagnosis of placenta praevia and other abnormal conditions of pregnancy.

There were no noteworthy complications either at the arteriography itself or following the examination. In none of the pregnant women did it induce labour; nor were the foetal heart sounds affected in the cases in which arteriography was carried out in the later stages of pregnancy.

SUMMARY

Percutaneous retrograde arteriography of the iliac artery was carried out in 80 cases of gynaecological disease, and in 21 pregnant women. In the majority of the gynaecological cases arteriography was combined with hystero-salpingography; this aided the diagnosis.

Most cases of myoma can be diagnosed by arteriography.

Arteriography of the iliac artery is shown to be a valuable aid in the differential diagnosis of myomata and ovarian tumours. In pregnant women it is possible to determine the site of the placenta by the procedure.

ZUSAMMENFASSUNG

Perkutane Arteriographie der Arteria iliaca wurde bei 80 Patienten mit gynäkologischen Erkrankungen und bei 21 schwangeren Frauen ausgeführt. In der Mehrzahl der gynäkologischen Fälle wurde die Arteriographie mit einer Hystero-Salpingographie kombiniert; hierdurch wurde die Diagnose erleichtert.

Die meisten Myome können mit Hilfe der Arteriographie diagnostiziert werden.

Es wird dargelegt, dass die Arteriographie der Arteria iliaca eine wertvolle Hilfe für die Differentialdiagnose zwischen Myom und Ovarialtumor ist. Bei Schwangeren ist es mit dieser Prozedur möglich, die Lage der Plazenta zu bestimmen.

RÉSUMÉ

On a pratiqué l'artériographie rétrograde transcutanée de l'artère iliaque dans 80 cas de maladie gynécologique, et chez 21 femmes enceintes. Dans la plupart des cas gynécologiques l'artériographie a été combinée avec l'hystérosalpingographie; ceci facilitant le diagnostic. La grande majorité des myômes peut être diagnostiquée à l'aide de l'artériographie.

L'artériographie de l'artère iliaque se trouve être d'une grande aide dans la discrimination entre les myômes et les tumeurs de l'ovaire. Chez les femmes enceintes il est possible de déterminer l'emplacement du placenta par ce procédé.

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ROENTGENOLOGIC DEMONSTRATION DURING MICTURITION OF PATHOLOGIC CHANGES IN THE FEMALE URETHRA

by

Björn E. W. Nordenström

A technique for cysto-urethrography in women, permitting of lateral films, has previously been described (3, 4). By employing the method, it is possible to demonstrate pathologic changes in the female urethra, easily overlooked with the usual technique.

For a proper appreciation of the pathologic cases now reported, the appearances of the normal urethra during miction should be kept in mind. Certain details of interest in this connection were previously described (5).

A well defined middle part of the urethra is recognizable in normal and many pathologic cases. This portion of the urethra is the widest, and

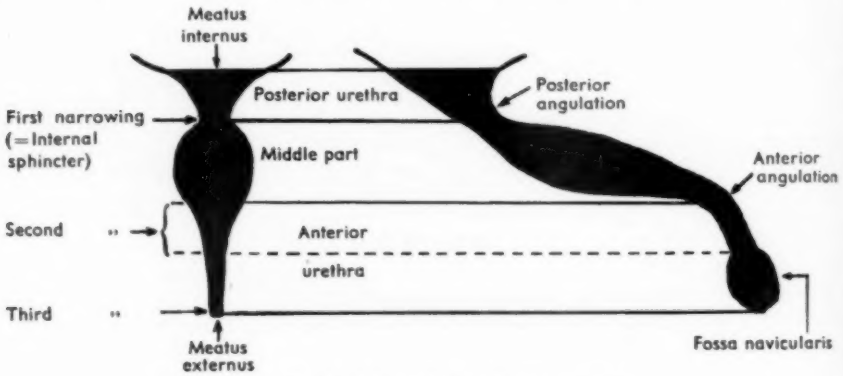

Fig. 1. Terminology of the female urethra.

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is situated between the narrowing of the posterior urethra and an angulation of the anterior urethra. Near this angulation the urethra is narrowed (second narrowing). The meatus externus forms the third narrowing. A navicular fossa is demonstrable in most female urethras. It appears to be a constant normal feature.

In the case reports which follow, the various parts of the female urethra are described as in Fig. 1.

Case Reports

(For measurement purposes a length of 3 cm is represented on the lateral films.)

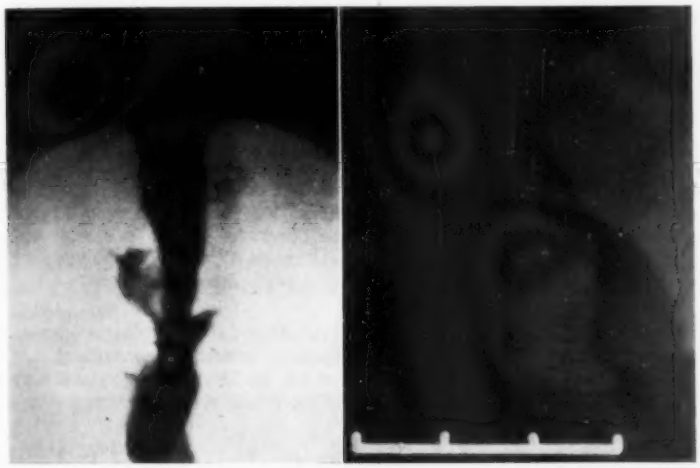


Fig. 2. Case 1. Straight and wide urethra with large navicular fossa.

Case 1. M. O. aged 42; nullipara. The patient, four sisters and mother suffered from stress incontinence from childhood. Plastic repair of the pelvic floor two years previously. No conscious sensation during micturation.

Whether a certain distension of the urethra or turbulence of the urine in the urethra is necessary for normal miction is unknown to the author. In any case, physical conditions do exist for the formation of 'urethral turbulence' in normal urethras. It would give a physical explanation of the existence of the various narrowings, dilatations and angulations of the urethra. Even the navicular fossa may from this point of view be given a certain physiologic function.

The urethra is short and wide. The anterior urethra is mainly formed by a large fossa navicularis. The course of the urethra is straight. The changes noted appear to be mainly congenital in origin. Due to the wide lumen and straight course the urethra would offer a comparably small resistance during miction. An operative narrowing of the external meatus might correct to some degree the disturbance of turbulence.

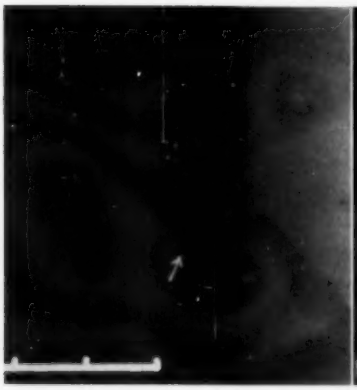


Fig. 3. Case 2. Angulation of the middle part of the urethra due to plastic repair of the pelvic floor.

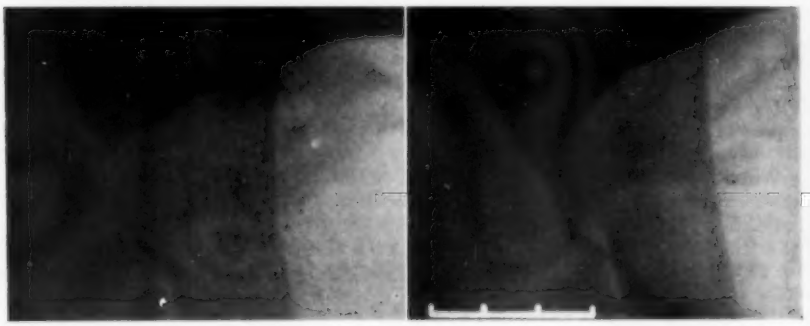
Fig. 4. Case 3. Pathologic angulation of the middle urethra (arrow).

Case 2. G. E., aged 52; two deliveries; stress incontinence during previous 15 years; continent after plastic repair of the pelvic floor — INGELMAN-SUNDBERG (2).

The urethra is rather long. It should be observed that a 'posterior angulation', situated in the middle part of the urethra, is the result of the plastic repair of the pelvic floor. It has nothing to do with the 'angulation' described by THOMSEN (7).

Case 3. J. F., aged 50; incontinent about 20 years. 1932 plastic operation of the posterior urethra; 1946: sling operation — SUNDE; remained incontinent.

The bladder base, the posterior and part of the middle urethra have a more anterocranial position than normal. This also causes a pathologic angulation of the middle urethra.



a. b.

Fig. 5. Case 4. a) lateral projection, rest; b) lateral projection, miction. Pronounced funnelling of the posterior urethra.

Case 4. D. S. aged 35; three deliveries; some months after the last delivery, 9 years previously: cysto-pyelitis; continent in recumbent position.

A pronounced 'funnelling' of the posterior urethra is seen, the first narrowing being completely absent. The funnelling is caused by a disturbance of the function of the sphincter internus.

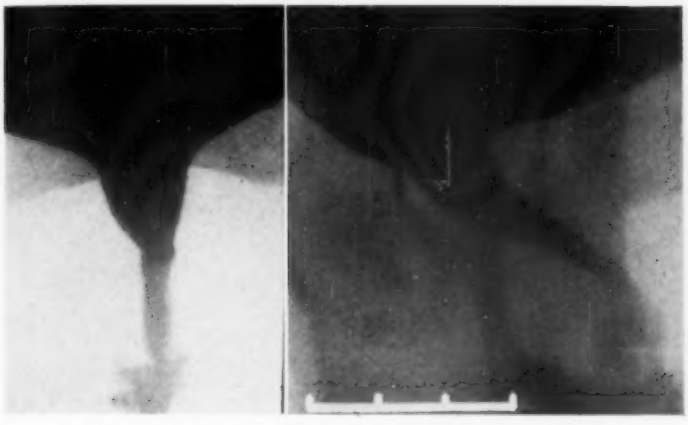


Fig. 6. Case 5. Funnelling of the posterior urethra.

Case 5. M. B., aged 30; two deliveries; vaginal prolapse following last delivery; stress incontinence.

Pathologic funnelling of the posterior urethra is present. The anterior urethra has a normal course and shape.

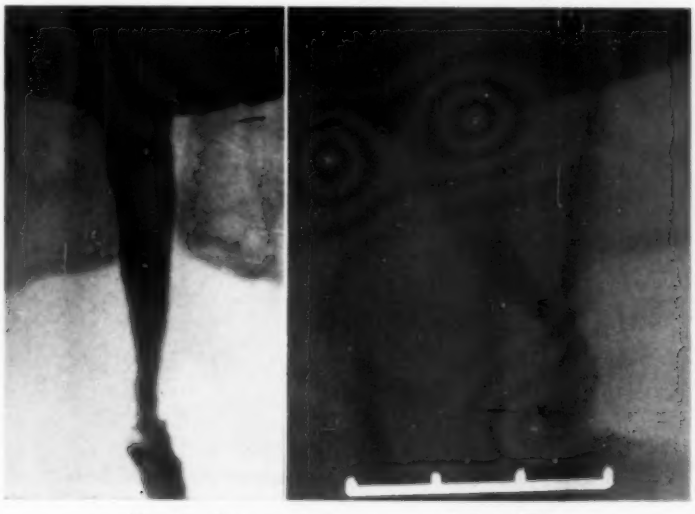


Fig. 7. Case 6. Less pronounced funnelling.

Case 6. S. S., aged 26; nullipara; stress incontinence. The posterior urethra has a rather straight course. The first narrowing is not seen. There is probably less pronounced funnelling of the posterior urethra than in Cases 4 and 5.

Case 7. L. H., aged 36; one normal delivery; continent; difficulty in emptying bladder.

Stricture of the middle part of the urethra. Dilatation of the urethra proximal to the stricture.

Fig. 8. Case 7. Stricture of the middle part.

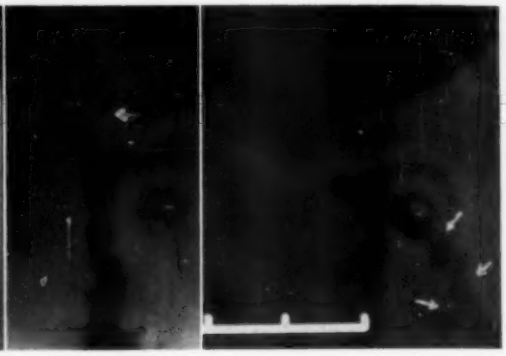


Fig. 9. Case 8. Multiple strictures.

Case 8. E. S., aged 43; nullipara; symptoms of cystitis for several years; continent. The walls of this urethra are irregular due to multiple strictures.

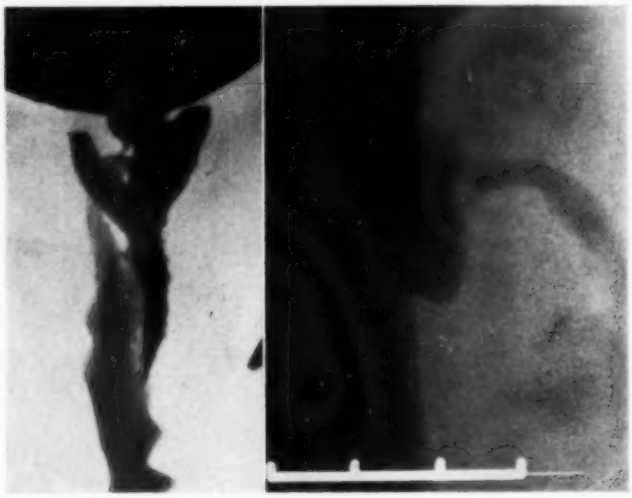


Fig. 10. Case 9. Paraurethral diverticula.

Case 9. A. S., aged 48 years; one normal delivery; gonorrhea 14 years previously; incontinent; pain during micturition.

There are paraurethral diverticula of the middle part of the urethra. It is often difficult to discover this pathologic change by urethroscopy (3).

Case 10. H. E. S., aged 54; nullipara; terminal dysuria during previous 3 years. Paraurethral diverticula of the middle part of the urethra.

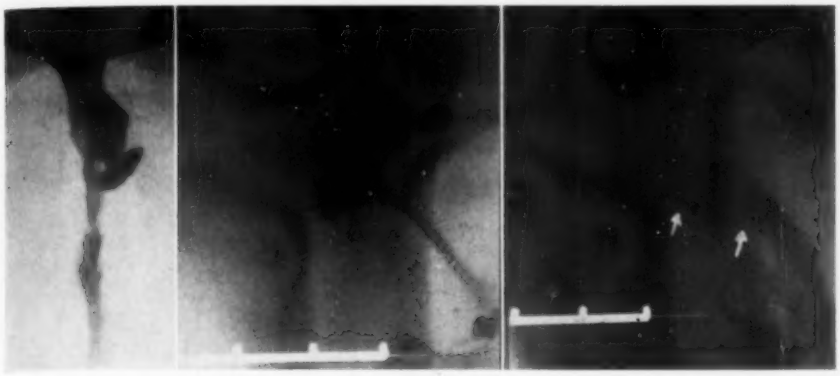


Fig. 11. Case 10. Paraurethral diverticula.

Fig. 12. Case 11. Irregular wall of the posterior urethra (arrows).

Case 11. A. L., aged 37; operated on for a diverticulum of the middle part of the urethra some years previously; symptoms of dysuria; continent.

The posterior wall of the urethral wall is somewhat irregular. This is due to strictures of the paraurethral tissue.

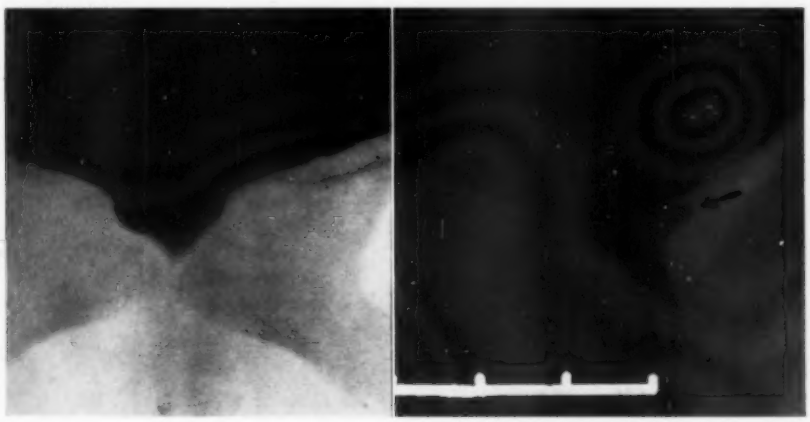


Fig. 13. Case 12. Appearance of the urethra after operative fixation of a muscle fascia to the anterior part of the posterior urethra (arrow).

Case 12. U. H., aged 21; nullipara; 1947 traumatic fracture of a vertebra causing incontinence, due to lesion of the spinal cord. At operation (laminectomy) 1948 compression of the cord between vertebra L. 1 and L. 2, was found; remained incontinent after operation. Continent after transplantation of a muscle fascia of the m. rectus abdominis which was sutured to the anterior part of the posterior urethra; micturation obtained by the aid of carbacoline.

The case represents an operative result of a woman suffering from incontinence due to a nervous disturbance of organic origin. (Infranuclear type of GIERTZ and LINDBLOM (1).)

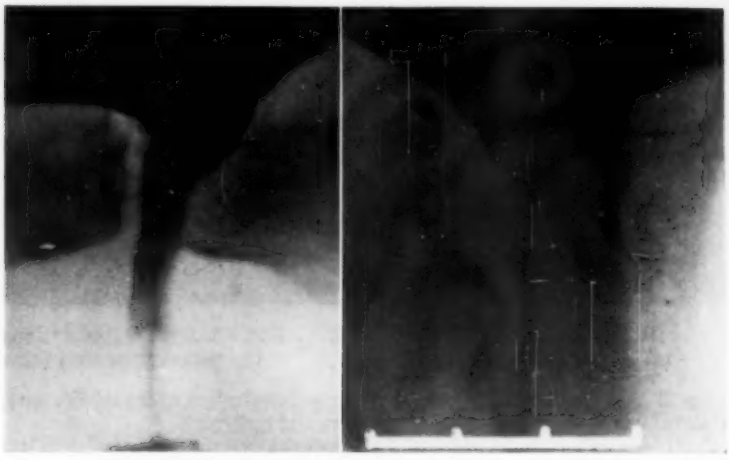


Fig. 14. Case 13. Strictures of the peri-urethral tissue of the posterior urethra. Straight and caudal course of the urethra.

Case 13. M. S.; aged 55; two deliveries; operated for vaginal prolapse five years previously; after operation suffered from stress incontinence; plastic operation of the posterior urethra twice during previous year.

The posterior urethra presents a pathologic shape due to strictures. The course of the urethra is straight and is directed downwards.

Case 14. G. M., aged 51; two normal deliveries in 1932 and 1938; stress incontinence during the previous ten years.

Case 15. T. P., aged 50; three normal deliveries — the last in 1931; stress incontinence during previous six years.

In Figs. 15 and 16 two cases of insufficiency of the pelvic floor in which the bladder moves in a dorsocaudal direction, more than normally, during miction. This causes a typical increase of the normal angulation of the anterior urethra.

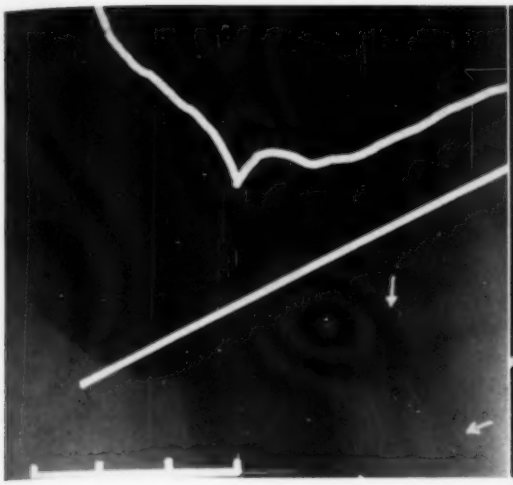


Fig. 15.

Fig. 16.

Figs. 15 (case 14) and 16 (case 15). Insufficiency of the pelvic floor. Typical increase of normal angulation (↓). Meatus externus (←). Irregluar white line: position of the bladder during rest. Straight lines: Part of the author's co-ordinate system for the topographic determination of the position of the urethra and the bladder.

Conclusions

The case reports suggest that the technique developed for urethrocystography during micturation has all the advantages of retrograde urethrocystography. At the same time the former gives the physiologic functional state of the urethra and the condition of the bladder and the bladder-neck are also easily studied.

SUMMARY

For the roentgenologic examination of the female urethra during micturition, a—p and lateral views must be obtained. The latter are the most important. A terminology of the female urethra is proposed. A description of certain pathologic changes in the urethra for the investigation of which the author's method of urethrocystography was employed, is given.

ZUSAMMENFASSUNG

Bei der Röntgenuntersuchung der weiblichen Urethra während der Miktion ist es notwendig, Aufnahmen in arterioposteriorer und lateraler Richtung vorzunehmen. Die lateralen Aufnahmen sind am wichtigsten.

Eine Terminologie der weiblichen Urethra wird vorgeschlagen. Gewisse pathologische Veränderungen der Urethra, zu deren Untersuchung die Urethrocystographietechnik des Verf. benutzt wurde, werden beschrieben.

RÉSUMÉ

L'urétrographie mictionnelle chez la femme nécessite une radiographie de face et une de profil. Celle-ci est la plus importante. L'auteur propose une terminologie (anatomique) de l'urètre féminin et donne la description de certaines modifications pathologiques de l'urètre mises en évidence par sa méthode d'urétro-cystographie.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR KNUT LINDBLOM),
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PRIMARY CARCINOMA OF THE THIRD PORTION OF THE DUODENUM

by

Lennart Kjellman

Primary cancer of the duodenum is widely agreed to be a relatively rare disease. The total number of cases mentioned in the literature amounts to about 400. Its incidence in autopsy material is stated by JEFFERSON, and by HOFFMAN and PACK, to be 0.04 per cent and 0.033 per cent, respectively; FELDMAN mentions the figure 0.003 per cent.

Opinions vary considerably regarding the share represented by duodenal cancer in the total figure for all forms of carcinoma of the intestines, incidences of from 0.3 to 4 per cent having been advanced. There is also considerable discrepancy in the statements with regard to the frequency of duodenal cancer in the total incidence of cancer of the small intestine; FELDMAN maintains that it only reaches a figure of approximately 3.5 per cent while EGER, HOFFMAN and PACK, and BERGER and KOPPELMAN (cited by KLINE and CULVER) conclude that the percentage is 45.

With regard to the percentage incidence of cancer in the individual portions of the duodenum, it is more or less generally held that the disease does not occur equally often in all the parts but attacks the second portion (the ampullary, peri-ampullary or peri-papillary part) in the vast majority of cases (57—81 per cent), while the third portion (below the ampulla or papilla) is less frequently affected. In addition it may be mentioned that the disease usually occurs between the ages of 50 and 70 and is two to three times more common in men than in women.

As regards the pathologic anatomy, adenocarcinoma is the dominating type among the various forms of cancer, and it may occur either as a polypous or as an infiltrating growth. If it occurs in the latter form, it is

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accompanied by stenosis and not infrequently also by ulcerative changes, in addition to which there is usually dilatation proximal to the constricted segment. Involvement of adjoining organs does not as a rule seem to take place until at a late stage in the disease, although according to KLINE and CULVER, infra-papillary cancer tends to metastasize earlier than cancer of other parts of the duodenum.

Carcinoma of the duodenum does not produce a definite and unequivocal syndrome. The subjective symptoms vary according to the nature and site of the disease, consisting, to begin with, of vague, gastro-intestinal discomfort in the form of loss of appetite, nausea, eructation, loss of weight and severe constipation. A less common symptom is pain, which is experienced for the most part in the right upper quadrant of the abdomen. Another early symptom, in the peri-ampullary form, is jaundice, due to stasis in the bile ducts. Vomiting as a sign of intestinal constriction does not occur until a slightly later stage when the disease has attacked the proximal part of the duodenum. On the other hand, when the distal part of the intestine is affected, vomiting does not, as a rule, occur until the terminal stages of the disease.

As regards the objective signs, there is usually tenderness to palpation in the epigastrium. A tumour, on the other hand, is distinguishable in about only one-third of cases, according to FELDMAN. Blood in the stools is a much commoner finding; when present it is usually a question of an occult haemorrhage; only in a very few cases is there massive melena, which originates from some large blood vessel that has been eroded as a result of the malignant changes. Anaemia is also present in a great many cases; its direct cause is, of course, to a large degree the aforementioned loss of blood, but a toxic effect due to the tumour is probably a contributory factor.

These vague symptoms and ambiguous clinical findings do not, however, permit of a definite diagnosis. The final proof is furnished by radiography, which is superior to other forms of diagnostic procedures in this condition.

As the roentgen appearances in duodenal cancer are very similar to those seen in other parts of the gastro-intestinal tract affected by a malignant growth, we may observe, in these cases, all degrees of central or eccentric constriction of the lumen, rigidity of the walls over an area corresponding to the extent of the tumour, obliteration of the normal markings of the mucous membrane and an irregular outline in the region. Further, the intestinal segment proximal to the affected area often displays either compensatory hypertrophy or secondary dilatation as signs that obstruction to the normal passage is present. In a few cases, however, these signs of stenosis are more or less entirely lacking despite the presence of a large tumour; this seems to be possible particularly with the

polypoid form of tumour, which may permit the contrast to escape past it (BUCKSTEIN).

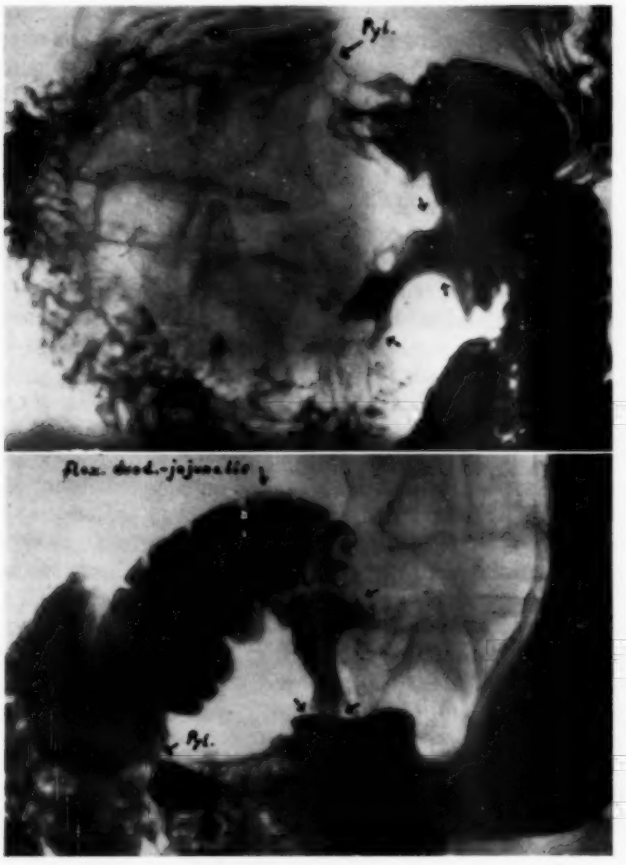
The earliest changes, the demonstration of which is of such vital importance for treatment, as well as prognosis, have unfortunately proved to be extremely easy to overlook. This is perhaps not surprising, in view of the fact that the disease is so rare — according to FELDMAN it is observed only once in every 30,000 gastro-intestinal examinations. However, when once a pathological process has been established, a number of differential diagnostic difficulties arise in the interpretation of the roentgen appearances. Because of the position of the duodenum, with its intimate relation to the bile ducts and pancreas, many changes both in these as well as in other adjoining organs may deform or encroach upon the intestine and give rise to appearances which are often very difficult or even impossible to distinguish from duodenal cancer. Roentgen signs resembling those produced by a tumour situated below the ampulla may be obtained, for instance, when arterio-mesenterial obstruction is present. The differential diagnostic significance which has been accorded to the different lengths of the constricted area in the case of a growth and of an inflammatory process must, furthermore, be said to have been somewhat exaggerated, seeing that the measurements given for these, a maximum of 5 cm and a minimum of 8 cm, respectively, are sometimes found to be the reverse.

The chances of being able to make a correct roentgen diagnosis of primary cancer of the duodenum are estimated very differently by various authors. Some investigators are inclined to draw too sweeping histopathologic conclusions, despite the fact that it has been found that occasionally even the microscopic examination may not furnish more than tentative information as to the origin of the disease. Others very rightly refrain from over-valuing the possibilities of differential diagnosis; they stress the importance of making an early diagnosis when the chances of effective treatment are still comparatively favourable and content themselves at that stage in establishing the presence of a tumour, a finding which naturally constitutes an indication for operation.

In order to eliminate the risk of overlooking a cancerous growth, for instance in the distal part of the duodenum — through which the barium usually passes rapidly — and, when the patient stands, is apt to be concealed by the contrast medium in the stomach — special attention should be paid to this region in every examination, as BERGENDAL has already pointed out. If the correct technique be employed and examinations made in the erect as well as in the supine and prone positions with adequate compression, it should not be difficult to obtain a clear and satisfactory representation of this part of the intestine.

Case Report

Female, aged 70; treated at the Medical Clinic of the Karolinska Sjukhuset in 1949 for vitium cordis, anaemia sideropenica and psoriasis. The roentgen examination of the oesophagus, stomach and duodenum was normal.



a.

b.

Figs. 1 a—b. Primary carcinoma of the duodenum causing a constriction close to the duodeno-jejunal junction but no prestenotic hypertrophy or dilatation. Right anterior oblique, supine (above); Left anterior oblique, prone (below).

She was admitted again in 1950 because of marked fatigue. Severe anaemia was now established and blood was repeatedly observed in the stools. Roentgen examination of the stomach, small intestine and colon revealed nothing abnormal.

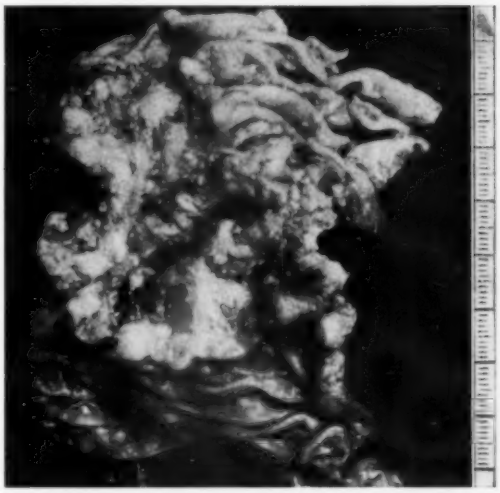


Fig. 2. The specimen after surgical removal.

In the summer of 1951 she began to experience an aching pain in the epigastrium and nausea but there was no vomiting. She had been slightly feverish and had lost much weight. Re-admitted in September as the blood values were steadily decreasing. On admission, examination of the heart revealed slow fibrillation and aortic insufficiency. The liver was palpable one finger's breadth below the costal margin; no masses palpable; no tenderness. Haemoglobin 46 %, red blood corpuscles 2.8 million, white corpuscles 3,600. Faeces: Weber test, positive. Roentgen examination of the stomach and duodenum revealed the following features: The wall of the stomach and the bulb were apparently normal. There was no obstruction to emptying. In the pars descendens, close to the duodeno-jejunal flexure, the lumen was narrowed for a distance of slightly over 4 cm, to a diameter of just under 1 cm. The outline was slightly irregular and the mucous membrane was not visualized. There was no evidence of any ulceration; no prestenotic dilatation noted. The signs pointed to the possibility of a malignant infiltration of the wall (Figs. 1 a and b).

A further study of the films from the preceding examination revealed that although the pathologic change was not evident in 1949 it was present but had been overlooked in the following year, and since then had increased considerably in size.

At operation on a diagnosis of probable cancer of the duodenum, intestinal haemorrhage and hypoproteinaemia, resection of the duodeno-jejunal flexure and the pancreas was performed in conjunction with duodeno-jejunostomy, terminostomy and drainage. There was no ascites. The stomach and proximal parts of the duodenum, as well as the liver and spleen, were normal. The duodeno-jejunal flexure was the site of a tumour the size of a hen's egg, markedly displaced upwards and backwards and in all probability invading the pancreas. The whole of the small intestine showed bluish discoloration from the presence of blood.

Presumably, the tumour had originated in the third part of the duodenum and injured a large vessel in the course of its propagation into the pancreas. The poor response to 14 blood transfusions given over a short period suggested that this assumption was correct.

For a few hours after operation the patient's general condition seemed to be fairly good, but deterioration soon set in and death occurred the following evening. Necropsy revealed incipient gangrene of the small intestine.

Microscopic findings: A section cut from the tumour displayed a fairly highly differentiated adenocarcinoma which in some places was growing in solid clumps. The intestinal mucosa appeared to pass over directly into the growth, a finding which suggested that the latter was probably duodenal in origin. The tumour had penetrated through the muscularis and serosa and into the parenchyma of the pancreas.

SUMMARY

A verified case of duodenal cancer, situated below the ampulla, is described and the literature on the subject briefly surveyed.

ZUSAMMENFASSUNG

Ein unterhalb der Ampulle lokalisierter, verifierter Fall eines Carcinoma duodeni wird beschrieben und ein kurzer Überblick über die einschlägige Literatur wird gegeben.

RÉSUMÉ

Description d'un cas vérifié de cancer du duodénum, situé au dessous de l'ampoule. Brève revue de la littérature sur ce sujet.

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FROM THE SURGICAL DEPARTMENT I, THE SAHLGREN HOSPITAL, GOTHENBURG, SWEDEN

FURTHER OBSERVATIONS ON 'CORTICALISOSTEOIDE' OR 'OSTEOID OSTEOMA'

by

Erik Moberg

In 1930 BERGSTRAND described in this journal two cases of 'osteoblastic' disease situated in a metatarsal bone and the first phalanx of a digit, respectively. In the first case the bone and in the second the whole finger were removed because malignancy was suspected.

In 1935 JAFFE described 5 cases of a similar pathologic process, mainly situated in short spongy bones. He interpreted this process as some kind of tumor growth. In 1940 JAFFE and LICHTENSTEIN published 28 further cases, several of which with involvement of the long bones. Through JAFFE's investigation the disease became widely known in the United States under the name of 'osteoid osteoma'. The characteristics of the disease were also clarified in many respects by this study. Due to interrupted communications during the war I did not know of this latter work when in 1941 I presented a personal series of 8 cases, 6 of which were localized to the diaphyses of the long bones, of a similar appearance. It seemed that these probably belonged to the same group of diseases as those with lesions in short spongy bones, described by JAFFE in 1940. As it was obvious that the question of a neoplasm did not arise, the term 'osteoma' seemed misleading, and I suggested in my article published in German the term 'corticalisosteoide' as being a more appropriate designation for this type of process. However, the name 'osteoid osteoma' has now been generally accepted in the U. S. A.

Since that time numerous cases have been reported from the United States (especially by JAFFE, 1945) but only a few cases from Europe. An interesting review of the literature by SHERMAN, 1947 (with an exhaustive bibliography), added 30 new cases to the previous number of 128 which has now been supplemented with further cases. Over and above the 8 cases which I previously reported, there seems to be only one other

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published in Scandinavia, by PALMER in 1945, the lesion being situated in the talus. It is peculiar that while a large percentage of the cases from the United States are reported as having the lesion situated in the short spongy bones and often in the vertebrae, involvement of this type of bone is seldom described in the European cases. Since 1941 I have observed four further cases; these illustrate the various forms under which the condition may be encountered.

Case Reports

Case 1. Male aged 18 years; shop-assistant. Complained of six months of pain and tenderness accompanied by swelling, particularly at night, in the anterior lateral region of the left foot; this had incapacitated him.

On examination marked swelling was noted over the antero-lateral aspect of the foot. There was distinct tenderness to pressure 1 cm proximal to the metatarsophalangeal joint of the fourth toe; plantar flexion of the toe was painful. The nocturnal pain was relieved by rest in bed. Roentgenographic examination (Fig. 1) disclosed thickening of the diaphysis of the fourth metatarsal bone. On the plantar aspect of the head of the bone, an area of destruction, the size of a pea, with a thin shell-like outline was noted. Periosteal thickening of the lateral surface of the third metatarsal and of the diaphysis

Fig. 1. Case 1. Eccentric situation of nidus in relation to sclerosis, which develops only in the periosteum-covered cortex and not at the joint. The arrow indicates periosteal thickening of adjacent bone.

of the first phalanx of the fourth toe was seen. At operation, a nidus twice the size of a pea, composed of a whitish-yellow, rather soft mass, not sharply demarcated from the surrounding normal bone tissue and lying under a paper-thin cortical shell, was found. This nidus was removed in toto.

Histologic examination (C. G. AHLSTRÖM) (FIG. 2). The yellowish-white nidus from the metatarsal head was built up centrally of osteoid bone trabeculae in plexiform arrangement, embedded in highly cellular connective tissue. This latter was the seat of numerous capillaries with engorged endothelial cells. Within and especially along the surface of the osteoid trabeculae scattered cells resembling osteoclasts were seen. In many areas close to and in the vicinity of osteoid trabeculae typical multinuclear osteoclasts in a state of disorganization were also noted. Within a small region the formation consisted entirely of highly cellular, newly formed, connective tissue and presented the first suggestion of the formation of osteoid tissue. No necrosis nor accumulation of amorphous collagen masses was noted.

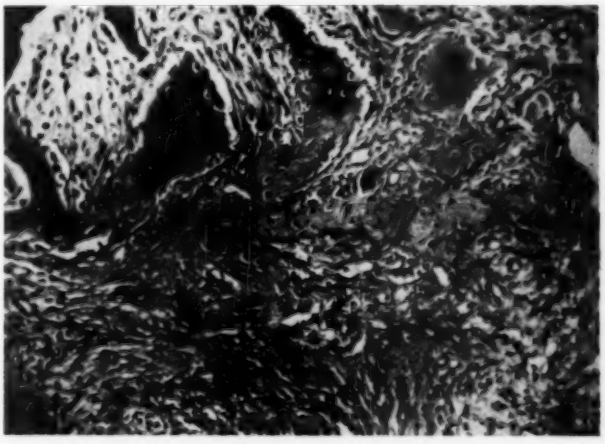


Fig. 2. Case 1. Microphotograph.

Peripheral to the central osteoid nidus, a zone of rather slender calcified trabeculae forming an osteoid framework was seen. The trabeculae were not disposed in lamellae, but surrounded by rows of osteoblasts and loose connective tissue, rather denuded of cells. In this area the vessels were fairly wide and thin-walled; only occasional osteoclasts were seen. The nidus was circumscribed peripherally by spongy bridges of lamellar bone of normal appearance.

There was no sign of tumor formation nor of an inflammatory process. There were no signs pointing to hemorrhage, no deposits of blood pigment or other changes to suggest a post-traumatic reaction.

To summarize, there was a restricted area of formation of osteoid tissue and calcification in addition to signs of a certain degree of destruction of the osteoid trabeculae. The observations did not reveal the specific nature of the process. It is, however, undoubtedly of the same character as BERGSTRAND's 'osteoblastic disease of bone'.

Immediate culture on bouillon, ascitic fluid agar and blood agar produced no growth.

Fig. 3. Case 2. Pea-sized rarefaction of a metatarsal bone with sclerosis of the entire diaphysis.

Fig. 4. Case 3. Nidus central to the cortical thickening.

Case 2. Female, aged 24, following trampling upon her right foot, experienced pain, worse at night. A roentgen examination elsewhere two months later suggested a fracture with callus formation. Thirteen months later the patient had a normal delivery; the pain in the foot increased during pregnancy.

On examination a slight local swelling over the fifth metatarsal bone as well as distinct tenderness proximal to the metatarsal head was noted. Roentgen examination revealed rarefaction, larger than a pea in size, of the left metatarsal bone with extensive sclerotic thickening along the entire diaphysis (Fig. 3).

The nidus with surrounding tissue was excised. Histologic examination revealed the same condition as in case 1. (The reader is referred to my paper in J. Bone & Joint Surgery, for further roentgen films and a microphotograph.)

Case 3. Male, aged 24, complained of pain of one year's duration at the base of the left second toe. The pain had not interfered with his working capacity and he had been able to take part in sports.

On examination slight swelling and tenderness to pressure over the affected area was noted. Roentgen examination showed a rarefaction the size of a grain of rice at the base of the first phalanx close to the articular surface (Fig. 4). Small periosteal deposits in the diaphysis close to the area of rarefaction were seen.

The local nidus with surrounding tissue was excised. The histologic picture was the same as in case 1.

Case 4. Girl, aged 14, for six months had complained of increasing pain in the left leg, especially at night. At several examinations elsewhere nothing abnormal had been found. Roentgen examination now revealed a marked periosteal thickening on the poste-

rior fibular aspect of the tibia; this was subsequently found to be progressing (Fig. 5). Localised rarefaction was only faintly demonstrable on the films, in spite of the most careful roentgenographic technique.

At operation a considerable amount of sclerotic bone was excised together with a small nidus measuring 3 × 4 mm. The histologic examination failed, however, to reveal this nidus and only dense cortical bone was seen; signs of inflammation were absent.

Fig. 5. Case 4. The nidus is only faintly visible through the dense cortical thickening (varying exposures).

The W.R. was negative, the S.R. not significantly elevated and other laboratory tests showed nothing of note in the four cases.

The central lesion was removed together with greater or lesser portions of surrounding sclerotic bone and healing by first intention was obtained in all the cases. The pain often disappeared amazingly soon. The symptoms did not recur and the patients were soon able to return to work; they have remained free from discomfort.

Discussion

There has been some argument as to whether this disease is a distinct clinical entity. BROWN & GHORMLEY (1943) and HELLNER (1950) maintained that the lesions are nothing more than a form of bone abscess. BRAILSFORD (1942) came to the same conclusion on the basis of a roentgenologic series. The vast majority of investigations, however, specially by trained pathologists (BERGSTRAND, JAFFE, DOCKERTY) hold that the disease is a distinct entity and is not of an inflammatory nature. This opinion seems at present to be almost generally accepted. The reason for disagreement among different authors seems to be that some have only had an opportunity of studying bone abscesses which, as will be demonstrated later, may roentgenologically closely resemble the so-called osteoid osteomata.

The cause and character of the condition are as yet quite obscure. Trauma can hardly be assumed to be a cause. For one thing, most patients have no history of trauma and secondly, the fact that the lesions usually lie in protected situations argues against such a possibility.

Neither BERGSTRAND's concept of the process as being derived from an islet of embryonic tissue nor JAFFE's tumor theory, are readily compatible with our recent knowledge of the process. The natural course of the condition, inter alia, argues against JAFFE's theory (cf. later). Fur-

thermore, the nidus is well-defined and is not composed of a homogeneous type of cell. The changes are definitely not inflammatory in character.

Clinically the disease is markedly chronic in character and always lasts for months or years; symptoms take the form of local pain, often nagging in character. Initially this pain is felt only after exertion but it soon increases and becomes unremitting. It is often typically nocturnal and may interfere considerably with sleep. A palpable tumor may in some cases be the solitary sign. The general condition is not appreciably affected.

Up to now no case of more than one lesion has been observed. LAPIDUS and SALEM reported having observed a dual lesion but there was some question as to the correct diagnosis of one of the lesions. The condition has been encountered in all parts of the skeleton, with the exception of the bones of the skull and the clavicle; in the long bones it is commonly situated in the diaphysis, although it has been found in the epiphysis (SHERMAN 1947).

The change is commonly manifested in the form of a slight projection of the bone under the normal skin. Edema is occasionally observed especially when the foot or other part subjected to heavy weight-bearing is involved. There may be slight tenderness to palpation or percussion.

At *operation* a sclerotic, often coarsely porous, cortical thickening is found; at the site corresponding to rarefaction on the roentgenogram, a central non-cystic nidus of softer consistency is commonly present. The size of the nidus varies from 1 millimeter in diameter to rather more than the size of a bean. The bone in this region is at times soft enough to permit easy removal with a spoon. In some instances the entire nidus may be removed in the shape of a small globe with a rough surface, although on the other hand the margins of the nidus are often interwoven into the surrounding dense bone tissue. There is never a sharply defined smooth bony wall. Pus and granulations are absent and there is no enveloping membrane.

Bacteriologically the process is sterile.

Macroscopic examination shows that the central nidus of the process, seen on the roentgenogram as a rarefaction, consists of softer tissue with a fibrous or friable bony structure.

The *microscopic picture* of the lesion has been described and illustrated in detail by BERGSTRAND as well as by JAFFE. The central softer area consists of osteoid tissue alternating with newly formed bone and older osseous trabeculae in irregular arrangement. The area between eburneous bone and osteoid tissue is highly vascularized giving the impression that intensive reconstruction is proceeding. Giant cells occur (See fig. 2). No signs of old hemorrhages have been encountered. There are no signs of inflammation, whether the symptoms are of several years' standing or

of recent date. It should be stressed that the histologic picture of osteoid osteoma shows complete absence of signs of inflammatory reaction. Case 1 affords an example of this; considerable swelling of the soft tissue around the lesion was present but inflammatory reaction was not microscopically demonstrable.

Histologic examination in various cases has shown a wide range of variation in the degree of the changes. In some cases the central osteoid areas are extensive, in others again there are but sparse streaks of osteoid tissue while the smooth and rather monotonous sclerosis is predominant. This variation is probably due to the lesion being at different stages of development in the various cases, although this question has not as yet been elucidated in detail (JAFFE 1945).

A rather similar picture from the histologic viewpoint may be encountered in cases of so-called fibro-osteoma situated in the bones of the skull. Clinically, however, the condition is so dissimilar that it should hardly cause difficulty in differentiation.

The normal course of the process has been followed and clarified to a certain extent by the aid of roentgen examinations (MOBERG 1951). As most cases have come to operation immediately after the diagnosis has been made, is has only been possible to carry this out in a small number of cases. It may be considered established, however, that the process develops from a minute focus, commonly in the cortex; the central nidus enlarges, destroying the normal surrounding bone, while the perifocal reaction takes the form of increasing sclerotic osseous thickening. The symptoms become more marked with the progress of the lesion.

When development has reached its peak (the nidus has not yet been known to exceed the size of a bean) the symptoms seem to subside over the course of one or several years and finally to disappear spontaneously; the roentgenographic changes persist for a very long time and only gradually diminish.

When the nidus is removed operatively (surrounding sclerotic bone need not be excised) the symptoms commonly disappear so rapidly that the patient is often free from pain the same day. If the central nidus is not excised radically the discomfort remains unchanged or recurs.

As the process, left to itself, may persist for some years and cause considerable discomfort, surgical intervention is indicated. Roentgen irradiation has been tried in various cases without success (STAUFFER 1944).

Not only is the pathogenesis and true nature of the disease obscure, but the differential diagnosis is also as yet incompletely studied. The preoperative diagnosis is essentially based on the history and the roentgen examination.

Roentgen diagnosis

Many earlier publications, inter alia a paper (1941) by the present author, describe the roentgen picture as characteristic. Increasing experience however has taught us that this is generally, although not always the case. Several cases have been encountered in which an erroneous preoperative diagnosis was made, due to other lesions giving similar roentgen appearances. Two distinct roentgenographic types of the disease occur: a) a type involving the diaphyses of the long and short bones, and b) a type involving the spongy bone, whether in the flat long or short bones.

a) When the process is situated in the diaphysis of the long or short 'tubular' bones, the roentgen appearances are in most cases characteristic. (Figs. 7 a; 3; and 6 d, e, g). The roentgen examination shows a fusiform tapering expansion and thickening of the cortex, which exhibits a smooth or finely granular, although sharply defined margin against the soft tissues. Spicula formation does not occur. The cortex may also show thickening on its medullary aspect, in some instances causing complete or partial obliteration of the cavity. A radiolucent centre or nidus is usually present in the dense cortex. This is frequently oval and ranges in size from a few millimeters to rather more than one centimeter in its longest axis. It may be located superficially, covered only by a paper-thin bony shell or be situated nearer the medullary cavity and expanding mainly in that direction. The margin is not entirely distinct, being sometimes rather blurred; there is no sclerotic border-line (Fig. 7 a). Varying roentgenographic technique is often necessary in order to obtain satisfactory visualization of the nidus through the often dense sclerotic thickening.

b) In spongy bone the picture is different: the surrounding sclerotic bone reaction seems to be usually far less marked or entirely absent. It may take the nature of a narrow, often eccentric, border zone. The central nidus in these cases is more commonly globular and of varying density, being sometimes more opaque in the centre with a less dense periphery, while in other cases the reverse is observed. In the spongy bones the process generally also seems to develop in, or adjacent to, the cortex. The case reported by PALMER with a nidus in the talus is typical of this group (Fig. 6 f).

The reason for the difference in the changes in the spongy bones and in the long bones seems to lie in the reaction of their periosteum-covered cortical surface. In Case 1, for example, in which the nidus was situated in the vicinity of the joint, the reactive formation of new bone extended exactly as far as the periosteum, whereas the cartilage-covered bony surface of the joint with no periosteum, although adjacent to the nidus,

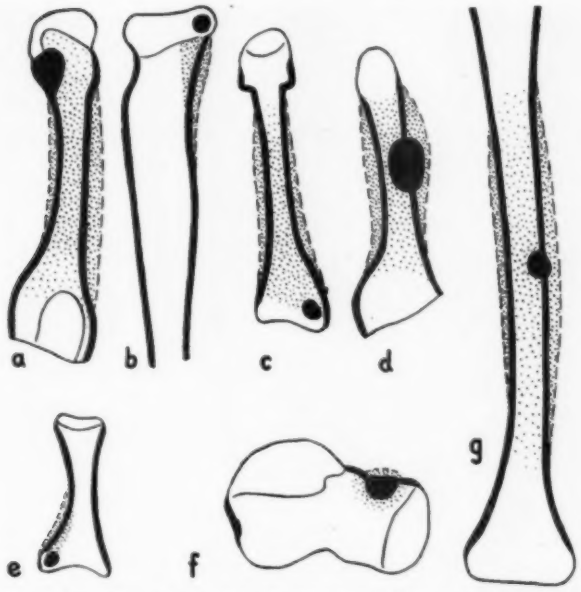


Fig. 6. New bone formation in relation to the periosteum covered cortex and 'nidus'. Sketches from roentgenograms. 'Nidus' — solid black. Periosteum covered cortex — heavy black lines. Perifocal new formation of bone — dotted.

a. Case 1, cf. fig. 1. *b.* Situated in head of radius (STAUFFER 1944). *c.* in metatarsal bone; *d.* case 2, cf. fig. 3; *e.* case 3, cf. fig. 4; *f.* in the talus; *g.* in the humerus.

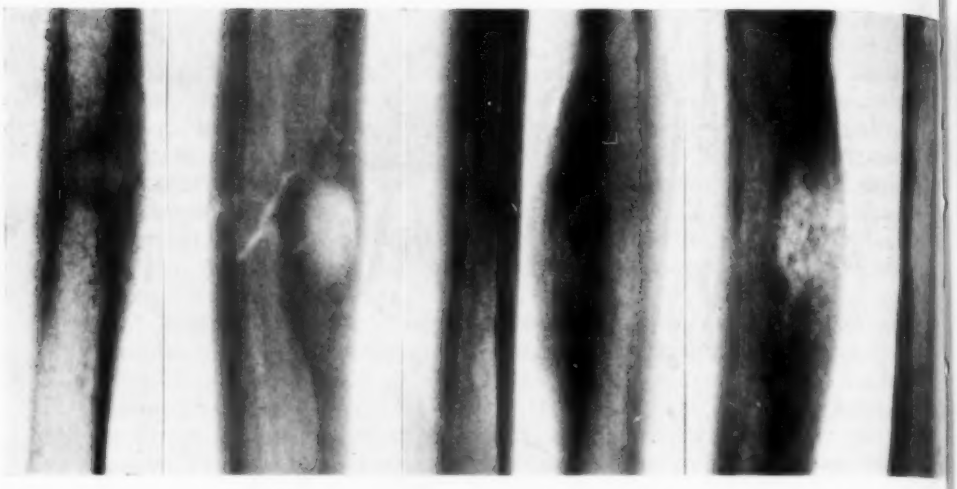
a, b, c & e. Eccentric situation of nidus. New bone develops in the presence of periosteum-covered cortex, but not in its absence. Cf. callus formation in fractures.

d & g. Nidus where the new bone can develop proximally as well as distally.

f. Slight bone reaction when nidus is sited in spongy bone with but limited periosteum covering.

showed no reaction. This factor causes a markedly eccentric situation of the nidus in relation to the reactive sclerotic process (Fig. 6 a). Similarly, the small nidus in the vicinity of the joint in Case 3 (Fig. 6 e) showed but a slight perifocal reaction, localized along the diaphysis.

The same relation between the sclerosis and the periosteum-covered cortical surface can be seen from the cases of other authors. STAUFFER (1944), for example, reported a case (Fig. 6 b) in which the nidus was situated in the head of the radius, but in which the reactive thickening was not demonstrable on the joint surface but only distally along one aspect of the epiphysis and in the diaphyses. Several cases with lesions in the scaphoid bone (which has but a very limited periosteum-covered surface) showed only a slight perifocal reaction. Many other examples of



a. b. c. d.

Fig. 7. Similar but actually different skeletal changes.

a) Osteoid osteoma of the humerus; b) Xanthomatous tumor of bone with fracture of the humerus (Microphotograph Fig. 9); c) Osteoid osteoma of the radius; d) Inflammatory change in the radius.

It should be possible to differentiate between the lesions shown in a) and b). The cortical reaction in b) is small in relation to the size of the centre, it is not symmetrical and a fissure is present. On the other hand, c) and d) can hardly be differentiated.

this type are found in illustrations presented in the literature. Figure 6 depicts schematic variants of this reaction, dependent on the various situations of the nidus in relationship to the periosteum-covered cortex.

It would thus appear that the situation and amount of the reactive process around the nidus are dependent essentially on the presence or absence of an adjacent periosteum-covered cortical bone surface.

As regards reactive bone formation, Case 1 is of particular interest, since the reaction is not restricted to the bone in which the nidus is sited but is also observed on two adjacent bones — the third metatarsal and the proximal phalanx of the fourth toe. To my knowledge, spread of the reactive process to adjacent bones has not previously been found in this disease, this change always having been restricted to one bone. It is debatable whether the periosteal thickening of the adjacent bones in this case was in the nature of a reactive process caused by extra strain, or directly by the nidus. A point in favour of the latter interpretation is the fact that the reaction of the third metatarsal bone was only found on its lateral aspect (in juxtaposition to the fourth metatarsal) and not on the

anterior and posterior surfaces where it would be reasonable to expect reaction, had it been a sequence of strain. It is at any rate suggested that reactive thickening of this kind may also occur on adjacent bones.

It may be difficult roentgenologically to differentiate the lesion from bone abscess, other inflammatory changes in the bones without abscess formation, certain forms of tumor and callus formation.

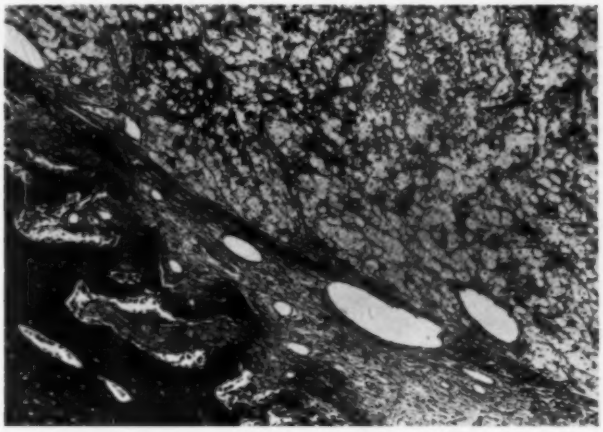


Fig. 8. Microphotograph of the xanthomatous tumor shown in fig. 7 b., which probably is a form of monostotic Schüller-Christian disease (eosinophilic granuloma). Numerous cells of foam-like appearance.

The differential diagnosis is founded to a large extent on the appearance of the nidus and the surrounding sclerotic process and on the relationship between them. The series of films reproduced in figures 7 and 9 illustrate this point as well as some of the difficulties that may be encountered.

In the long bones particularly, the nidus may be surrounded by such a dense sclerotic mass that it may be difficult to distinguish it in detail, or even to see it at all. Accordingly, it is impossible to distinguish between different processes from the appearance of the central area of rarefaction alone. In figure 7 a the nidus is of typical appearance, with a blurred outline and a radiolucent centre. Yet it cannot be definitely distinguished from the centre in figure 9 a, which depicts a bone abscess. Likewise a comparison of the osteoid lesion in figure 7 c with the case of osteitis without abscess shown in figure 7 d, reveals no characteristic difference.

a. b. c. d.

Fig. 9. The difficulties of differential diagnosis are evident from the following cases.

a. Cortical abscess of tibia. Granulation-filled cavity evacuated. Growth of staphylococci. Histologically, infiltration of leukocytes and lymphocytes. *b*. Cortical abscess of tibia. Cavity 3 × 3 mm filled with firm granulation tissues evacuated. Histologically, inflammatory focus with formation of granulation tissue and pus. *c*. Syphilitic osteitis. *d*. Stress fractures of fibula with callus formation.

In a) the centre has caused too little reaction in surrounding tissue to be the nidus of osteoid osteoma. The same is true of b) and there the periosteal reaction is also too diffuse and cloudy. Nor should it be possible to misinterpret c) because of the elongation of the centre and the uneven periosteal reaction, nor d) because of the thin deposits and lack of a central rarefied area.

In so-called osteoid osteoma, the width and length of the surrounding sclerotic process is fairly proportional to the size of the nidus. Figure 9 a shows a bone abscess. If it had been an osteoid osteoma, the large centre would probably have been associated with much longer and wider cortical thickening than the localized, mere suggestion of reaction shown in the film. In osteoid osteoma, the periosteal reaction is symmetrical when the process develops near the middle of a long bone. An uneven cloudy structure, which characterizes the inflammatory process shown in fig. 9 b, does not occur. Nor does one see the irregular structure present in syphilitic osteitis (fig. 9 c). The cortical line does not become so heavily delineated as in the case of callus formation following a stress fracture

shown in fig. 9 d; this also lacks central rarefaction so there should not be much chance of confusion here. However, it has happened that fractures of this kind in the metatarsus have caused mistakes. The xanthoma shown in figure 7 b also differs in several respects from an osteoid lesion. The rarefied centre is large and irregular and the cortical thickening is far too thin and localized to be secondary to such a large central rarefaction situated in the middle of a long bone. There is not great increase in the width of the bone. The medullary cavity is still wide. Lastly, there is a fissure of the bone, doubtlessly of a pathologic nature. As far as is known, no fractures occur in the pathologic bone in cases of osteoid osteoma.

It should therefore be quite possible to differentiate along these lines between the processes shown in figs. 7 a and 9 a, *i. e.* so-called osteoid osteoma and cortical bone abscess.

In fig. 9 b, both the insignificant cortical thickening and the cloudy periosteal reaction outside it point to an inflammatory process. Finally, the roentgenogram of syphilitic osteitis (fig. 9 c) shows a too irregular and elongated central rarefaction and a too irregular periosteal reaction to be compatible with osteoid osteoma. On the other hand, it is probably impossible to differentiate correctly from the roentgenologic appearances between the conditions shown in figs. 7 c and 7 d. In both cases the central rarefaction is visualized only as a few radiolucent streaks and in both cases the even and elongated periosteal reaction is quite compatible with the presence of an osteoid osteoma. Fig. 7 c depicts the latter lesion, fig. 7 d, a frankly inflammatory process. This shows that some cases of inflammatory changes in the cortex, with or without abscesses and sequestrae, may present appearances very similar to that of so-called osteoid osteoma. JAFFE questioned this possibility in 1941 but in 1945 stated that he himself had made the same observation.

There may be other skeletal changes which have more or less similar roentgenologic appearances to osteoid osteoma. Larger series must be collected in order to determine to what degree osteoid osteoma varies in roentgenologic appearances.

It is thus still impossible to make a definite diagnosis by roentgenologic means in every case. However, together with the generally characteristic clinical course, the result of the roentgenologic examination often decides the question of operation.

As was pointed out in 1941, and has been stressed by several authors, the disease is not particularly rare. From a clinical point of view, the greatest risk with the lesion is that it may be mistaken for malignancy and lead to amputation.

SUMMARY

Four cases of so-called osteoid osteoma are reported and a short review is given of our present knowledge of the disease, the various forms in which it appears, its clinical course, histologic picture and treatment.

The possibilities of roentgenologic diagnosis are discussed, as well as the difficulties which may be encountered in distinguishing the lesion from bone abscess and other bone diseases. In this connection it is pointed out that the condition takes different forms in long and spongy bones and the explanation for this is given. The manner in which the sclerosis around the nidus develops in various situations is described.

ZUSAMMENFASSUNG

4 Fälle des sogen. Osteoidosteomes werden geschildert. Eine kurze Übersicht über unser augenblickliches Wissen über diese Krankheit, über die verschiedenen Formen, in denen sie klinisch verläuft, über ihr histologisches Bild und die Behandlung wird gegeben.

Die Möglichkeiten der Röntgendiagnose werden besprochen, ebenso die Schwierigkeiten, denen man bei der Trennung der Krankheit vom Knochenabszess und anderen Knochenerkrankungen begegnet. In diesem Zusammenhang wird hervorgehoben, dass die Erkrankung in langen und spongiösen Knochen in verschiedenen Formen auftritt und die Erklärung hierfür wird abgegeben. Die Art und Weise, auf welche die Sklerose um das Bett herum in den verschiedenen Situationen entsteht, wird beschrieben.

RÉSUMÉ

Présentation de 4 cas d'«ostéome ostéoide». Courte revue de nos connaissances actuelles sur cette maladie, les différentes formes sous lesquelles elle se présente, son évolution clinique, son histologie et son traitement.

Étude des possibilités de diagnostic radiologique et des difficultés que l'on peut rencontrer pour distinguer cette lésion de l'abcès osseux et d'autres affections osseuses. L'auteur attire l'attention sur les aspects différents que prend l'affection dans les os longs et dans les os spongieux, et en donne l'explication; il décrit la façon dont la sclérose qui entoure le foyer se développe suivant les différents sièges de la lésion.

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AIR EMBOLISM EIGHT HOURS AFTER VENTRICULOGRAPHY

A Case Report

by

F. Heppner

Complications following ventriculography may appear immediately, or affect each tissue layer in turn. Infections of the scalp, skull, meninges, or brain substance itself, and their sequelae have been known.

Mechanical alteration of the nervous matter by the tapping may cause local brain oedema. For this reason the old method, originally suggested by DANDY, of occipital trephine openings has been generally given up in favour of the parieto-occipital approach. In this way oedema of the calcarine cortex, *e. g.* transient amauroses, may be avoided.

Injury to the pial or ependymal vessels may lead to unwanted bleeding. The stimulus of the introduced air on the choroid plexus causes hypersecretion of CSF, and raises the intracranial pressure. Finally there have been cases reported in which tapping of a brain sinus is said to have caused air embolism.

The origin of this last-mentioned complication is difficult to explain with due consideration of the technique used nowadays. In such cases there was presumably an atypical formation of blood vessels or, as seems more probable, the procedure was not suitable.

With increasing experience and development of surgical procedures such incidents to-day have become rare. It therefore seems worth reporting a case in which, despite an ordinary procedure and the use of all known precautionary measures, an air embolism under strange circumstances arose.

Case report. The patient, a female, aged 58 at time of death. During the year previous to examination there was progressive deterioration of memory and concentra-

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tion ability. In the previous month she had severe frontal headache, increasing drowsiness and squinting; she neglected her domestic duties and became morose and reserved.

Condition on admission: Head turned to the right and movements from this position resisted; moderate neck stiffness; frequent wiping of the nose with the right hand; facies dolorosa; the right hand often pressed against the forehead with a suffering gesture. Eyes most of the time closed. Strabismus divergens. Paresis of the right abducens nerve. Pronounced dizziness. Spasm and motor restlessness of the right arm. Passive movements of the left arm imitated by the right. Bilateral forced grasping and groping, more marked with the left arm. Reflexes equal on both arms. Trömner's sign negative. Could not carry out finger-nose test. Left ankle- and knee-jerk slightly exaggerated. Oppenheim positive on both sides. Fundus: both discs flattened, on the left extravasation and bending of the vessels.

Treatment: 50 % glucose and 10 % saline solution with $^1/_8$ mg Strophantin intravenously. Euphylline. Magnesium sulphate enemas. After this treatment the patient, on being spoken to now answered weakly with "yes" or uttered inarticulate monosyllabic words.

Two trephine holes for ventriculography were made in local anaesthesia (1 % novocaine-adrenaline) parasagittally and 12 cms above the occiput: the dura was opened by a cross-shaped incision and the pia electrocoagulated leaving an opening just large enough for the Cushing needles. A puncture was made on each side pointing towards the lateral border of each orbit. At a depth of 6 cms the lateral ventricle was reached; CSF clear and under high pressure; eighty ccs were withdrawn and sixty ccs of air introduced proving that there was free communication between the ventricles. Both scalp wounds were closed with interrupted silk sutures through all layers of the scalp.

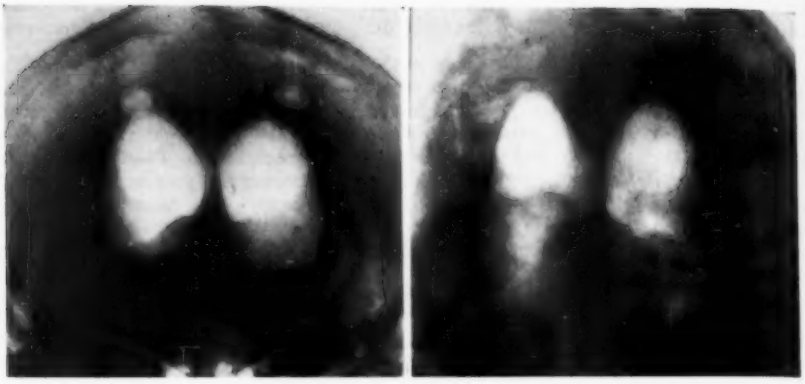
There was no disturbance of any kind during the operation and no bleeding. As a result of the withdrawal of CSF the patient was distinctly more responsive to her surroundings.

Ventriculogram (Vogler): There is marked hydrocephalus of both lateral ventricles. A small apple-sized tumour extends from the medial basal to the anterior part of both lateral ventricles. In the region of the frontal horn of the left ventricle, there is an additional small filling defect. On the lateral film the extension of the tumour and its sharply defined intraventricular growth is also seen. Despite changing the position of the patient several times no air could be brought from the lateral ventricles to the third ventricle or to the subarachnoid space. The ventriculography reveals a subfrontal, central, fairly medially situated tumour with extension into the septum pellucidum and the floors of both frontal horns, as well as partial blockage of the foramina of Monroe (See fig. 1).

The tumour was considered inoperable and palliative decompression was planned. The patient was put to bed with the upper part of the body a little raised, and was given 150 gms of 50 % glucose and $^1/_8$ mgm strophantin intravenously.

Eight hours after the ventriculography sudden death occurred.

Autopsy findings: Haematoma of the scalp in the region of the ventriculography burr holes. The corresponding openings of the dura are situated above the brain sulci on both sides. Delicate pial vessels closed by electrocoagulation clots noted. The brain convolutions are very widened, the sulci flattened. The puncture canals of the ventriculography open on both sides into the superior aspect of the posterior horns. On the left side an ependymal vein of 2 mms diameter lies opened. The CSF in both lateral ventricles is slightly blood-stained. On the base of the brain, projecting caudally, somewhat over the surface, tightly fitting the chiasm, there is a small apple-sized tumour, the central



a. b.

c.

Fig. 1. Central tumour with blockage of foramen of Monroe a) A. P. view. b) Halfaxial view. c) Lateral view in supine position.

mass lying in the septum pellucidum and reaching to the fornix. On the left the tumour protrudes as a small cyst, filled with blood-stained fluid into the frontal horn of the left lateral ventricle. When the heart was opened under water, air bubbles were released from the right ventricle. Right atrium and ventricle: very dilated. Struma nodosa. Myoma of uterus.

Section of the brain after fixation in formalin showed a subependymal vein opened in the region of the superior portion of the posterior horn of the right lateral ventricle and beside the opening of the tapping canal. It shows a larger diameter than the corresponding vein in the left lateral ventricle. In the course of the tapping canal in the white matter and the cortex no opening of a large vessel is seen; there is no venous injury in the region of the tumour. It can therefore be supposed that the air embolism occurred through one of the two opened veins situated subependymally in the area of the tapping canals in the lateral ventricles (PROBST).

Microscopic examination: Glioblastoma multiforme with development of a cyst, projecting into the lateral ventricle ependyma under a thin layer of glia.

Discussion

Eight hours after a ventriculography carried out in the typical parieto-occipital manner the patient suddenly died. The death was caused by air embolism. The question why the embolism did not occur during the ventriculography may be thus answered: The lobe-shaped laceration of the venous wall probably kept the vessel shut like a valve. A sudden increase of the venous pressure, perhaps by coughing, opened this valve. Because of the patient's position with the upper part of the body a little raised, the venous pressure was negative and the air contained in the ventricle was aspirated into the vein. Autopsy excluded the other possibility — that communication between the circulatory and the ventricular system by the pathologically vascularized tumour had occurred.

Conclusions

The principle that even a minor surgical procedure represents an "ultima ratio" and should, if possible, be replaced by more conservative measures seems to us especially appropriate when applied to ventriculography and is confirmed by the reported case. Therefore we conclude: Ventriculography is only indicated where a complete blockage of CSF is encountered and no ventricular filling is to be attained by means of encephalography. In all other cases we prefer ascending encephalography by the lumbar route as modified by LINDGREN; by its employment cerebral herniation is definitely prevented. In 87 pneumographic ventricular examinations which included 52 cases of expanding lesions, not a single incident was noted. This method also proves successful in children; they should be given 3—5 gm pentothal sodium intramuscularly.

Whenever it be impossible to operate on patients with increased intracranial pressure immediately after ventriculography, that is to say by reason of inoperable tumours, coma or poor general condition for instance, a recumbent position in bed is recommended. In such a case the increase of intracranial pressure must be regarded as the lesser evil and be treated by osmotherapy rather than by raising the upper part of the patients' body in bed. Only in this way the decrease in the intravenous tension to below zero can be avoided and a possible intravenous aspiration of ventricular air, as happened in our case, prevented.

SUMMARY

The author discusses the complications which may arise following ventriculography and an illustrative case of air embolism is reported. He prefers to employ ascending encephalography (LINDGREN's method) which does not produce sequelae.

ZUSAMMENFASSUNG

Der Verf. diskutiert die Komplikationen, die im Anschluss an die Ventrikulographie auftreten können und berichtet über einen illustrativen Fall mit Luftembolie. Er bevorzugt die aufsteigende Encephalographie (Lindgren's Methode), welche keine unangenehmen Folgen aufweist.

RÉSUMÉ

L'auteur étudie les complications qui peuvent survenir après la ventriculographie et rapporte un cas démonstratif d'embolie gazeuse. Il préfère employer l'encéphalographie par voie lombaire (méthode de LINDGREN) qui ne donne pas de séquelles.

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FROM THE CENTRAL CLINICAL LABORATORY, ST. ERIK'S HOSPITAL, STOCKHOLM, SWEDEN

THE MECHANISM OF THE EXCRETION OF RENAL CONTRAST SUBSTANCES

by

Bertil Josephson

Of recent years our knowledge of the excretory mechanism for the group of substances to which the most important renal contrast media belong has increased considerably. It may therefore be of interest to discuss this mechanism in connection with the question of the normal visualization of these media in roentgen examinations of the kidneys.

Before giving an account of recent investigations on the renal excretion of the substances in question it will first be necessary to discuss very briefly the present views on the formation of urine and renal excretion in general. These are matters familiar to all who are engaged on or interested in renal questions.

The kidneys consist of a great number of nephrons. There are over 1 million of these in each human kidney. From the arterial blood which (Fig. 1) reaches the malpighian tuft via the arterioli, about 15—20 per cent of the plasma is filtered out into Bowman's capsule. The filtrate is then conveyed via the convoluted tubules into the collecting tubules and thence to the renal pelvis. The glomerulus-filtrate constitutes, as we have said, 15—20 per cent of the plasma supplied to the kidney in healthy

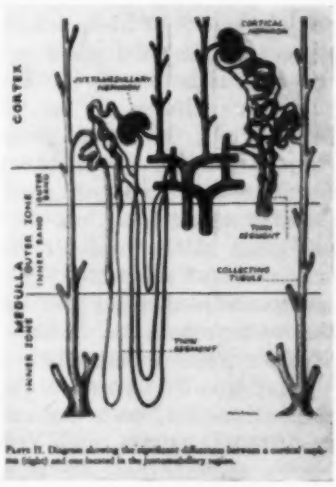

Fig. 1. Schematic picture of the structure of the kidney. (From Homer Smith.)

Submitted for publication, April 24, 1952.

persons; but in cases of hypertonia it may be as much as 30 per cent or more, and in cases of acute or chronic nephritis be reduced to 5 per cent or less. It contains, in the same concentration as in the plasma-water, all the ultrafiltrable substances existing in the plasma. It is thus a matter of a simple ultrafiltration, the blood cells, protein and lipoids being impeded and remaining in the blood in the capillaries. A contrast medium, for instance, which has been injected into the bloodstream should be filtered out in the same concentration in the filtrate as in the plasma. On the other hand high-molecular substances, such as proteins or lipoids, do not pass through the filtration membranes except in minute amounts; this implies a certain restriction to the filtration of contrast media, since a part of them is always bound to the plasma proteins.

In a subject with healthy kidneys, altogether about 120 ml plasma per minute, or about 1,700 liters every twenty-four hours, are filtered in the glomeruli. With the help of inulin or creatinine we may obtain quite a fair idea of the exact amount. In this connection I would stress that the urea clearance test, which is still used in many hospitals to judge glomerular filtration, is a poor and unreliable one.

Of the 1,700 liters which are filtered every twenty-four hours, not more than about 1 liter, or between 0.5 and 1 per cent, is excreted as urine. This is due to the fact that in the course of its passage through the tubuli almost all the ultrafiltered water is resorbed back into the blood, which through filtration in the glomeruli has become concentrated. Along with the water, the greater part of the substances dissolved in the filtrate are also resorbed into the blood, which thus recovers nearly its original composition. In this way all the sugar (except in diabetics) and most of the salts etc. are resorbed. However, a few substances are either not at all or only to a very slight extent resorbed. Among these are creatinine, inulin and the contrast media. This means that through the water-resorption in the tubuli they are concentrated in the course of their passage some 100—200 times.

But this by no means explains the whole process of excretion of the contrast media. As a matter of fact it describes only a small part of it. In 1923 MARSHALL and VICKER discovered that certain dye-stuffs *can also be excreted* from the blood by the tubular epithelium into the urine passing from the glomeruli through the lumen of the tubuli. It has since been found that the more important renal contrast substances are also excreted in this way. This, the tubular excretion, has been and still is the object of many and important investigations. The tubular excretion appears to be a sort of detoxification process for the organism. Only a few rather unimportant substances of those resulting from normal metabolism (certain sulphuric acid esters and glycuronic acids) are supposed to be excreted in this manner. On the other hand, a number of sub-

stances not belonging to the body are excreted through the tubular excretion — if added to the blood. Among such are the more important renal contrast media and *e. g.* hippuric acid, penicillin etc. The effectiveness of a renal contrast medium may be said — apart from its contrast-density — to depend upon the extent to which it is excreted tubularly.

None of the known contrast media attains a tubular excretion like that of di-iodopyridon acetic acid; this was introduced in 1921 by BINZ under the name Per-Abrodil, but is nowadays best known under the American designation 'Diodrast'; this latter substance is actually the diethanolamine-salt of di-iodopyridon acetic acid. There are, of course, several other renal contrast media which are excreted by the same mechanism although to a lesser extent, *e. g.* mono-iodohippuric acid. In this paper, however, only diodrast will be discussed. In our investigations we have used Umbradil from AB Astra Ltd, Södertälje, Sweden. This preparation appears to be a chemically pure solution of the diethanolamine-salt of di-iodopyridon acetic acid.

The tubular excretion is a much more variable and labile function than the glomerulus filtration, which, as already pointed out, is a simple process of ultrafiltration in which a certain part of the passing plasma is filtered out, the percentage in one and the same individual being fairly constant. Thus the amount of diodrast filtered is directly proportional to the diodrast-concentration in the plasma.

As regards the tubular excretion the case is otherwise. The tubular excretion of diodrast increases, as also does the amount filtered, proportionally to the plasma-concentration as long as this is low — under 15—20 mg (counted as diodrast iodine) per 100 ml in healthy persons. But when the concentration exceeds this limit the tubular excretion reaches a maximum, 25—50 mg per min., which is then not exceeded (SMITH, GOLDRING & CHASIS 1938). Consequently, the total diodrast-excretion is not proportional to the plasma-concentration, but increases more steeply with rising concentration when the latter is low than when it is high. This is illustrated in Fig. 2, which represents a test on a healthy person. In nephritic states the limit at which the concentration reaches its maximum, the so-called 'depression limit', is lower than in normal conditions (JOSEPHSON, BUCHT, EK & WERKÖ 1952). In this connection, however, I would point out that English research groups (EGGLETON & HABIB 1950) consider that they have shown that very high concentrations of diodrast are able to block the tubular excretion completely, so that it ceases altogether or is reduced very considerably below the maximum. These results however, have been obtained in experiments in animals; we have no definite proof that such an obstruction could be brought about in man for the simple reason, amongst others, that in human subjects it is scarcely possible to retain such high concentrations

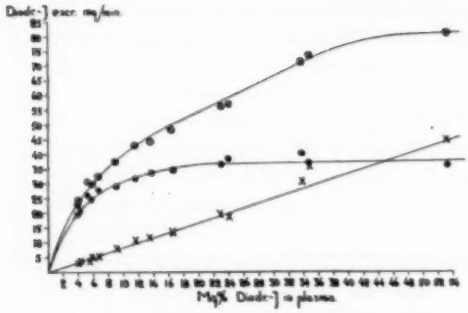

Fig. 2. Contrast excretion in a healthy human subject after intravenous single injection of 40 ml 35 per cent Umbradil.
○ — total excretion in mg iodine per min.
● — tubular excretion in mg iodine per min.
× — filtered contrast in mg iodine per min.

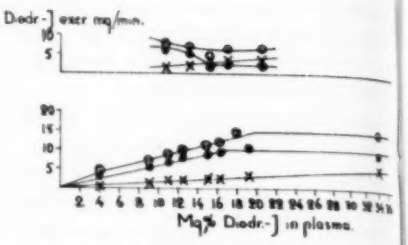

Fig. 3. Excretion in two patients with chronic nephritis after a single intravenous injection of 20 ml 35 per cent Umbradil. Signs as in Fig. 2.

for more than a very short time. We believe, however, that we have made an observation that might be interpreted as representing such an obstruction or one of a similar kind when we have given relatively large injections of diodrast to patients with severely damaged kidneys (JOSEPHSON 1947). Fig. 3 is an example of such a result from two patients with severe nephrosclerosis. The glomerulus filtration is not affected by the blockage.

What, now, will be the effect on the excretion of diodrast when given in a large single injection? The high initial diodrast concentration of the plasma will decrease according to a logarithmic curve; the poorer the renal function, the flatter will be the curve. In Fig. 4 we may for the time being ignore the first period after the injection. Despite the high plasma-concentration we find in this period a lower excretion, owing to the fact that during its commencement the diodrast-free urine that was in the tubuli and the renal pelvis at the moment when the injection was made, is excreted. But then we see that during the three first periods, when the plasma-concentration was over the depression limit, the tubular excretion was nearly constant, in spite of a falling concentration. The filtered amount of diodrast, on the other hand, was more proportional to the concentration. When the plasma-concentration sank below the depression-limit the tubular excretion was no longer maximal, and it, too, sank in proportion to the plasma-concentration. This means that with very high plasma-concentrations the filtration will dominate over the tubular excretion. With low concentrations the filtration and the

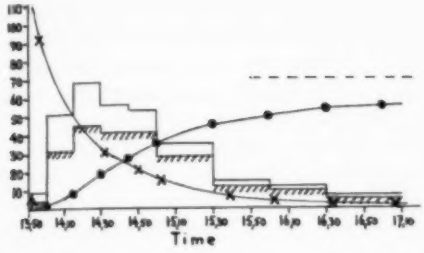

Fig. 4. Excretion in a healthy human subject after injection of 40 ml 35 per cent Umbradil. The excretion divided into periods.
▨ = filtered diodrast
□ = total excretion.
The difference between the levels corresponds to the tubular diodrast-excretion.
● = total amount of excreted diodrast iodine after injection.
× = the plasma-concentration of diodrast iodine.
= total amount of injected diodrast iodine.

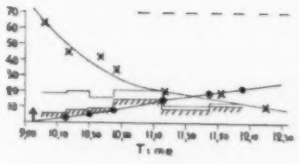

Fig. 5. Excretion in a patient with chronic nephritis after intravenous injection of 20 ml 35 per cent Umbradil. Signs as in Fig. 4.

tubular excretion proceed together. In nephritic states the conditions are more irregular, probably owing to the fact that the tubular excretion may be more or less blocked. In Fig. 5 we see a case in which the tubular excretion was maximal but low.

To what extent will the facts adduced above have an effect upon the relationship between the size of the injection and the amount of diodrast excreted? This may be seen in Fig. 6, which shows the results from a large series of experiments in rabbits. These tests were made in

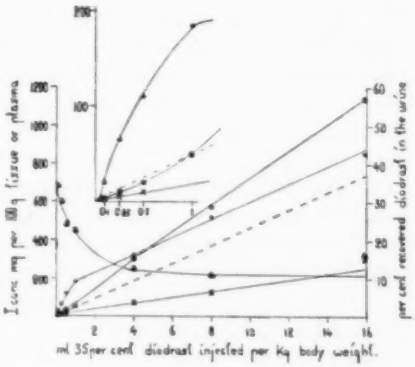

Fig. 6. Concentration-curves and excretion-curve for Umbradil after intravenous injection in rabbits of varying amounts of 35 per cent Umbradil. All the animals were killed 10 min. after the injection, the urine being collected at the same time. Each point is the mean of 10—15 experiments.
○ = plasma-concentration of diodrast iodine.
● = concentration in renal tissue.
× = concentration in hepatic tissue.
△ = amount of excreted diodrast, expressed as a percentage of the amount injected.

animals, as some of the doses were of an order of magnitude that cannot be employed in human subjects. Each point corresponds to the mean of 10 to 15 animals that were killed exactly 10 minutes after injections of Umbradil varying from 0.1 to 16 ml 35 per cent solution per kg body-weight. What chiefly interests us in this connection is the curve for the plasma-concentration and the curve showing what part of the amount injected was excreted in the urine within 10 minutes. We find that the plasma-concentration is directly proportional to the amount injected. The percentual excretion of diodrast, on the other hand, is much higher after small injections than after large ones. When 0.1 ml per kg body-weight was injected, about 40 per cent of the amount injected was recovered in the urine within 10 minutes. This was because the plasma-concentration was under the depression-limit, so that the tubular excretion was not limited, but was high in relation to the amount of medium injected. When the latter, and with it the plasma-concentration, was increased, the depression-limit was exceeded, so that the tubular excretion became stagnant at its maximum and only the glomerulus filtration continued to increase with the greater dose. When the concentration, and with it the filtration, became very high, the tubular excretion was entirely negligible in relation to the amount filtered. But as this amount is constant in relation to the plasma-concentration, the total amount excreted also approached a constant value if reckoned as a percentage of the amount injected. This percentage, as will be seen, was much lower than with small injections. In other words: *if one gives large doses one does, certainly, obtain a large total excretion but not anything like proportional to the excretion after small injections.* This rule does not hold for patients with severely damaged renal parenchyma. In these cases the tubular epithelium is generally so affected that its excretory capacity is very low and often negligible even with low plasma-concentration. For this reason the excretion is practically proportional to the filtration and the plasma-concentration right from the outset.

In this connection it ought to be mentioned that the diuresis has not the slightest effect upon the total amount of diodrast excreted. A low diuresis therefore gives a high concentration and a high diuresis a diluted urine, since the total amount of diodrast found is independent of the diuresis. With a low diuresis one thus obtains a contrast-rich urine. This is of course a very important point to be borne in mind when examining patients with poor renal function and low excretion of diodrast.

We are not afraid of giving diodrast to patients with considerably impaired renal function (JOSEPHSON 1947), though in such cases we generally reduce the dose. Of course, our experience cannot be compared with that of roentgenologists; but not in a single one of our cases, including several with fairly poor kidneys, have we observed any serious

or prolonged symptoms or side-effects in connection with the diodrast injections. It must be considered unnecessary and meaningless to add anti-histamine preparations or other so-called antidotes to the diodrast. The sensation of heat, occasionally accompanied by slight nausea, that is often observed, is by no means specific for diodrast. It is experienced after most large injections of strongly hypertonic solutions.

When deciding which cases call for a reduced dose, many are guided by the non-protein nitrogen of the blood. This, however, is a rather poor indicator of the state of the kidneys. Far better is the inulin or creatinine clearance, but if this has not been performed one may obtain a fair idea from the serum creatinine. If this be higher than about 1.4—1.5 one should exercise caution.

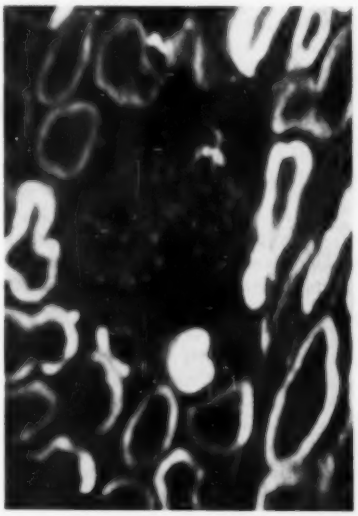

Fig. 7. Microroentgen photograph of the kidney of a rabbit 10 min. after injection of 8 ml 35 per cent Umbradil per kg body-weight (Arne Engström). In the middle of the photograph a glomerulus surrounded by cross-cut tubuli. The walls of the tubuli are full of contrast medium (white).

Finally, I would mention that the tubular epithelium has a certain capacity to become charged with diodrast, which it harbours as the latter passes from the blood to the tubular lumen. Fig. 7 shows a microroentgen photograph, taken by ARNE ENGSTRÖM, of a kidney from a rabbit in which we had injected a large dose of diodrast. In this photograph the light parts are contrast-filled. One sees how the tubular walls are full of contrast. It cannot at present be decided to what extent the visualization of the kidneys in intravenous urographies is due to this charging of the cells or to an accumulation of contrast-containing urine in the tubuli.

SUMMARY

The principles of renal excretion are described. A filtration of the plasma takes place in the glomeruli of the kidneys although certain substances including the contrast media are also excreted by the tubular epithelium to the passing urine. The significance of this mechanism in urography as well as the effect of the amount of contrast medium administered is discussed. Experiments in animals and trials in healthy and diseased human subjects permit conclusions regarding the excretion of the media to be made.

ZUSAMMENFASSUNG

Die Prinzipien der renalen Ausscheidung werden beschrieben. Das Plasma wird in den Glomeruli der Nieren filtriert, aber gewisse Stoffe, unter denen die Kontrastsubstanzen, werden auch vom Epithelium der Tubuli abfiltriert. Sowohl die Bedeutung dieses Mechanismus für die Urographien wie der Einfluss auf die injizierte Menge Kontrastsubstanz werden diskutiert. Tierversuche und Experimente an gesunden und nierenkranken Menschen gestatten Konklusionen über die Ausscheidung der Kontrastsubstanzen.

RÉSUMÉ

L'auteur décrit les grandes lignes de l'excrétion rénale. La filtration de la plasma a lieu dans les glomérules rénaux à l'urine passante, bien que certaines substances, parmi lesquelles les produits de contraste, soient aussi excrétées par l'épithélium tubulaire. L'auteur étudie l'importance de ce mécanisme dans l'urographie ainsi que l'effet de la quantité de produit de contraste administrée. Des expériences sur des animaux et sur des sujets sains et malades permettent de tirer des conclusions sur l'excrétion des produits de contraste.

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FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR: PAUL JACOBY), THE COUNTY AND CITY HOSPITAL, ODENSE, DENMARK

EPIPHYSEAL SEPARATION AS THE CAUSE OF ABNORMAL REMODELLING OF BONE

(Formation of an "Umbauzone")

by

Johannes Thoms

A change in the physiologic remodelling of bone, so that the equilibrium between bone formation and bone absorption is disturbed, may be recognized in the roentgenogram as a more or less pronounced, local or diffuse decrease or increase in the density of the osseous tissue.

The interpretation of the various pictures of bone atrophy has been a much-debated subject. In 1900, SUDECK reported cases of acute bone atrophy following inflammatory processes. In 1901, KIENBÖCK claimed that posttraumatic atrophy was of the same nature as that occurring after inflammation. From a review published by HERFORTH it appeared that trauma was often the exciting factor; of 203 cases of Sudeck's atrophy, 91 were found to be posttraumatic.

The initial roentgenologic sign of incipient acute bone atrophy is a zonal decalcification in the metaphyses of the long bones, adjacent to the epiphyseal lines (HALDBO, SCHINZ et al.). This process may be recognized when the calcium content has been reduced by 10 per cent (BAASTRUP), or when a difference between the calcification of the Haversian system and that of the interstitial lamellae has occurred (LANDOFF). However, injury to the epiphyseal line seems also occasionally to be responsible for the development of this phenomenon, without this being part of or constituting the initial phase of a Sudeck atrophy proper. The two cases presented below are illustrative examples.

Case 1. A boy, J. J. S., aged 13 years, was treated as an out-patient (Rec. No. 10755/50) on Nov. 15, 1950. Earlier in the day he had fallen and injured the left forearm. Swelling, marked tenderness and a dorsally open angulation a few centimetres above the wrist were noted.

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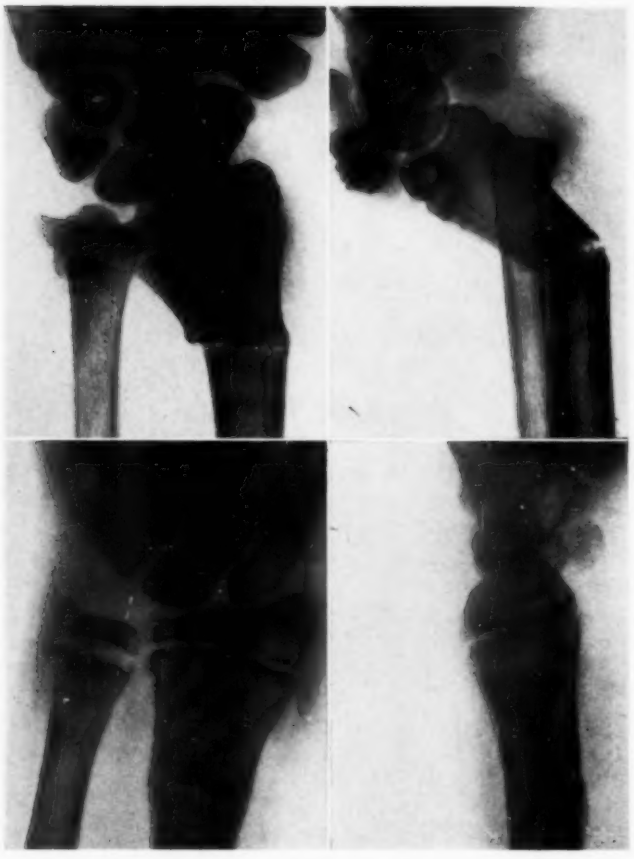

Fig. 1, Case 1. a. Left wrist of 13-year-old boy. Transverse fracture of the radius and complete separation of the distal epiphysis of the ulna. After reduction the ulnar epiphyseal line appeared normal with a maximum width of 3 mm.

b. Check-up roentgenogram, taken four months later. A metaphyseal band of lessened density is seen in the ulna, and the width of the epiphyseal line has increased to 6 mm.

Roentgen examination (fig. 1 a) showed a transverse fracture of the radius, approximately 1.5 cm proximally to the epiphyseal line, with considerable displacement and complete separation of the distal epiphysis of the ulna. A control roentgen examination after reduction and immobilization revealed almost perfect position; the epiphysis of the ulna showed a good anatomic relationship, and the epiphyseal line appeared normal with a maximum width of 3 mm.

Fig. 2, Case 2. a. Right ankle of 13-year-old boy showing apparently normal conditions after trauma.

b. Check-up roentgenogram, taken four months later, showing pronounced widening of the distal epiphyseal line of the tibia due to a metaphyseal band of lessened density of a width of up to 8 mm. Periosteal proliferation, notably on the medial side.

A follow-up roentgenogram (fig. 1 b), taken four weeks later (Dec. 11), showed distinct incipient callus formation at the site of the radial fracture. The ulnar epiphyseal line was represented as a 6 mm wide band caused by a less dense zone in the metaphysis; the proximal demarcation of the zone was somewhat irregular.

Case 2. A boy, A. T. M., aged 13 years, was treated as an out-patient (Rec. No. 3152/50) on June 16, 1950, after having injured the right foot while playing football

earlier in the day. Moderate swelling and tenderness of the right ankle-joint, particularly around the medial malleolus and at the anterior margin of the tibia, and indirect tenderness were present. The range of movement of the ankle-joint was unrestricted.

The roentgenogram (fig. 2 a) showed apparently normal appearances.

The patient was treated with a supportive bandage for a fortnight, after which the symptoms diminished, although the discomfort persisted to a varying degree. He was seen again on Oct. 17 as the condition had become aggravated. It was stated that he had not been exposed to any trauma since the first examination. Moderate swelling and tenderness were still present, notably at the anterior margin of the tibia.

Now, four months after the injury, the roentgenogram (fig. 2 b) showed a somewhat irregular but distinct widening, up to 8 mm, of the distal epiphyseal line of the tibia, due to a metaphyseal zone of lessened density. Proximally, the demarcation was very irregular and slightly blurred. In addition, thickening of the metaphyseal periosteum was seen, notably on the medial side.

Later control roentgenograms (last on Dec. 11, 1950) showed varying degrees of opacity of partially confluent, dense areas in the previously almost uniformly clear metaphyseal zone and distinct thickening of the periosteum.

Roentgenograms of other epiphyseal lines showed normal conditions.

Discussion

As shown by LANGER, the metaphyses and epiphyses have greater vascularity than the other parts of the bone. This is the cause of the special reaction of the zones of growth to various affections and in particular pathologic conditions. In his experimental studies on mechanically caused transformation processes in bones, MÜLLER showed how the patho-anatomic process develops in the zones of growth. The loops of the vessels of the canals of the bone marrow become short and sparse. The intermediary cartilage increases in thickness. The columnar arrangement of the cartilage cells disappears, and the cells lie in clumps or very irregularly. The enchondral ossification is inhibited or abolished, so that predominantly osteoid tissue develops instead of new bone tissue. RIEDER demonstrated that these changes are due to a secondary congestion following a primary lesion to the vessels in the zone of growth. A local acidosis develops, resulting in an increase of the quantity of ionized calcium, and the calcification of the osteoid tissue is delayed or fails to appear. According to FRUTIGER, this process is excited via a centre in the spinal cord through a parasympathetic nerve.

It must be presumed that this development occurred in the cases reported above. In case 1, the vessels were damaged by the complete dislocation of the epiphysis to such an extent that the calcification was delayed and the abnormally wide osteoid zone developed in spite of correct reduction and immobilization. In case 2, it would appear that a primary injury was caused to the zone of growth (epiphyseal separation without dislocation). Its tolerance limit for strain was thus reduced, and normal weight-bearing acted as a constant secondary irritant, resulting in the development of the wide calcium-free osteoid zone.

Comments

The underlying process may develop anywhere in the bone tissue. The condition may also be encountered in adults, frequently affecting the previous zone of growth (BECKER). MÜLLER compared the condition to the changes in the metatarsal bones in 'march fracture' and to the lines of Looser in rickets. Corresponding to the march fractures of the metatarsal bones, HANSSON and NORDENTOFT reported cases of insufficiency fractures of the tibia and fibula. In an experimental study, NAGURA also demonstrated a patho-anatomical analogy between various injuries to bones due to excessive strain.

In some conditions affecting the general health, such as the osteopathy of famine disease (LAMY et al., HOTTINGER et al.), leukemia (BICHEL) and osteomalacia, renal rickets, syphilis and scurvy, similar osseous manifestations may be encountered.

In the differential diagnosis tumors, tuberculosis and osteomyelitis must be considered, since these conditions are often situated in the zones of growth of the bones and may result in growth disturbances (BÜRGSTEIN).

An epiphyseal separation with slight or no displacement may give rise to diagnostic difficulties. Forssell's lamella sign is essentially of interest in separation of the distal epiphysis of the radius (WERENSKIOLD). As shown in the cases presented here, a zone of lessened density in the metaphysis may be caused by epiphyseal separation, and the sign may thus be of importance in the diagnosis of doubtful cases. The correct diagnosis of epiphyseal separation is very important because the condition may be followed by deforming growth disturbances (GILL et al., BÜRGSTEIN).

Finally, it may be mentioned that changes in the zone of growth is of special importance in the diagnosis of incipient epiphyseal separation of the head of the femur, as emphasized by PERKINS and KLEIN et al.

SUMMARY

Two cases of epihyseal separation, causing abnormal remodelling of bone, are reported. This is evidenced roentgenologically as an area of lessened density of the zone of growth (formation of an 'Umbauzone'). The patho-anatomic process is discussed and the diagnostic and differential diagnostic importance of the sign is emphasized.

ZUSAMMENFASSUNG

2 Fälle von Epiphysenlösung, die eine abnorme Umformung des Knochens zur Folge hatten, werden berichtet. Diese ist röntgenologisch sichtbar als ein Bezirk geringerer Dichte der Wachstumszone (Bildung einer »Umbauzone»). Der pathologisch-anatomische Prozess wird diskutiert und die diagnostische und differentialdiagnostische Bedeutung des Symptomes wird betont.

RÉSUMÉ

Description de deux cas de décollement épiphysaire causant un remodelage anormal de l'os; ceci se traduit radiologiquement par une aire de moindre densité de la zone de croissance (formation d'une »zone de remaniement«). L'auteur étudie ce processus-anatomo-pathologique et souligne l'importance de ce signe pour le diagnostic positif et le diagnostic différentiel.

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AUS DER RÖNTGENABTEILUNG DES SANKT-FRANZISKUS KRANKENHAUSES (VORSTAND: DR. J. E. J. RESINK) UND DER ROTTERDAMER ANSTALT ZUR BEKÄMPFUNG DES RHEUMATISMUS (LEITER: DR. P. VAN DER MEER), ROTTERDAM, HOLLAND

ZUR RÖNTGENOLOGIE DER SACROILIAKALEN GELENKE

von

J. E. J. Resink

Für die Frühdiagnostik der Bechterewschen Krankheit ist die Röntgenuntersuchung der sacroiliakalen Gelenke besonders wichtig.

Die Aufnahmetechnik erfordert eine genaue Kenntnis der Anatomie dieser Gelenke. BARSONY und SCHULHOF haben diese eingehend untersucht. Von ihren Studien ist Folgendes besonders wichtig.

Die sacroiliakalen Gelenke konvergieren in craniocaudaler Richtung. Sie stellen keine ebenen Flächen dar, sondern zeigen meistens neben mehreren Unebenheiten zwei charakteristische Knickungen. Diese Knickungen befinden sich etwa auf der Grenze zwischen den cranialen und caudalen Vierteln. Hierdurch können wir drei Teile unterscheiden: *A.* die cranialen Teile. *B.* die Mittelteile (dies sind die grössten Teile) und *C.* die caudalen Teile. *A.* und *C.* laufen parallel mit der Sacrumachse: die *B.*-Teile konvergieren immer in caudaler Richtung. Was die Lage hinsichtlich des sagittalen Querschnittes anbelangt, sehen wir meistens folgendes: die *A.*-Teile laufen parallel zueinander oder konvergieren ein wenig nach ventral; die *B.*-Teile konvergieren nach dorsal; die *C.*-Teile stehen meistens parallel zum sagittalen Querschnitt. Also konvergieren die grössten Teile der Gelenke in dorsaler Richtung. Dies ist für die Röntgenologie von grosser Wichtigkeit. Die Lage der Gelenke in Hinsicht auf die Horizontalebene wird durch die Beckenneigung bestimmt und kann sehr verschieden sein. Je stärker die Beckenneigung, je grösser ist der horizontale Schnitt und je kleiner der vertikale Schnitt des Gelenkes.

Es gibt beträchtliche Unterschiede, sowohl der Grösse der Gelenkflächen als auch hinsichtlich der Lage der Gelenke. Die Konvergenz nach caudal und nach dorsal kann sehr verschieden sein, auch eine Asymmetrie zwischen rechts und links kann es geben. Wichtig ist weiter, dass die Pars sacralis iliaca sich ein gutes Stück nach mediodorsal erstreckt und das sacroiliakale Gelenk grösstenteils bedeckt.

Aus dem Obenstehenden ergibt sich, dass bei einer gewöhnlichen

Bei der Red. am 21. I. 1952 eingegangen.

Röntgenaufnahme in anterio-posteriorer Richtung die Gelenkspalte nicht der Länge nach von den Röntgenstrahlen getroffen wird und dass das Gelenk grösstenteils von der Tuberositas iliaca verdeckt ist. Infolge der Konvergenz der Gelenke nach dorsal werden auf der Aufnahme von jedem Gelenk zwei Spalten dargestellt, nämlich eine sogenannte „hintere" Spalte und eine etwas mehr lateral gelegene „vordere" Spalte. Das untere Ende des Gelenkes zeigt auf der Röntgenaufnahme öfters nur eine Spalte weil es hier meistens mit der Sagittalebene parallel läuft. Durch die mehr oder weniger starke Neigung des Beckens ändert sich die Höhe des Gelenkes und auch die Figur, welche auf dem Röntgenfilm von den Spalten dargestellt wird. FORESTIER, ROTES-QUEROL und JACQUELINE haben die verschiedenen Bilder, die so entstehen können, eingehend beschrieben. Sie unterscheiden vier Typen: A. Den vollständigen Typus (beide Spalten bilden einen ovalen Ring); B. Den Y-Typus; C. Den V-Typus und D. Den Typus mit nur einer sichtbaren Spalte.

In den letzten 20 Jahren sind verschiedene spezielle Aufnahmemethoden für die sacroiliakalen Gelenke beschrieben worden. Dabei ist man von folgenden Grundsätzen ausgegangen:

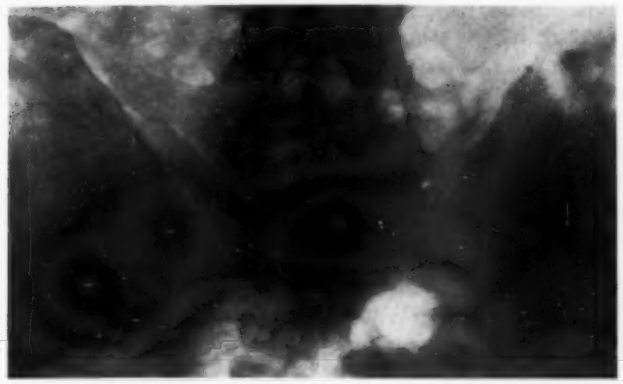
A. Das Becken wird mehr oder weniger um die Längsachse gedreht. Bei einer solchen sogenannten halbseitlichen Aufnahme soll der Zentralstrahl durch die ganze Länge der Gelenkspalte hindurchgehen und die Tuberositas iliaca grossenteils lateral vom Gelenk projiziert werden. Der Winkel, unter dem die Drehung des Beckens erfolgt, wird sehr verschieden angegeben: nach *Dittmar* 30—35°, nach *Huberny* 45°, nach *Ghormley* und *Kerklin* 32°, nach *Morton* 45° und nach *Kovacs* 15—25°. Einige dieser Aufnahmetechniken hatten auch die Absicht, eine bessere Einstellung der kleinen lumbalen Zwischenwirbelgelenke zu erzielen.

B. Die lumbosacrale Lordose wird nach Möglichkeit beseitigt, wodurch das Sacrum parallel zur Aufnahmeebene zu liegen kommt und die sacroiliakalen Gelenke möglichst in ihrer grössten Länge dargestellt werden (SAMUEL und TESCHENDORF; KOVACS).

Auch wurden diese Massnahmen kombiniert angewandt (GALLAND und DE LAS CASAS, BARSONY und SCHULHOF). Mit diesen Methoden beabsichtigte man insbesondere, auch eine bessere Möglichkeit zur Beurteilung des fünften Lendenwirbels und des Zwischenwirbelloches zwischen L. V und dem Sacrum zu erhalten.

Mit keiner der obenerwähnten speziellen Aufnahmetechniken erreicht man jedoch eine ideale Darstellung der Gelenkspalten der sacroiliakalen Gelenke, da man ja nie im voraus wissen kann, wie stark die Gelenke nach dorsal hin konvergieren oder wie ausgeprägt die Lendenlordose ist.

Da es sich herausgestellt hatte, dass die Übersichtsaufnahme im allgemeinen zur Beurteilung der sacroiliakalen Gelenke nicht genügt



a.

b.

Abb. 1. a. Übersichtsaufnahme sacroiliakaler Gelenke.
b. Unter Durchleuchtung angestellte Aufnahmen desselben Kranken. Normales Bild.

und auch alle andere Aufnahmemethoden nicht zu einem befriedigenden Resultat führten, haben wir einen ganz anderen Weg eingeschlagen. Wir machen die Aufnahmen dieser Gelenke unter Durchleuchtung, wie es JAEGER (1949) vorgeschlagen hat. Hierbei steht der Patient hinter dem Fluoreszenzschirm und zwar mit dem Rücken dem Schirme zugewandt. Von jedem Gelenk wird eine besondere Aufnahme gemacht. Der Patient wird so lange um seine Längsachse gedreht bis man bei der Durchleuchtung eine deutliche Gelenkspalte beobachtet. Da die Gelenke nach dorsal hin konvergieren, wird der Patient so gedreht, dass die Seite, von der eine Aufnahme gemacht wird, sich in einiger Entfernung vom Fluoreszenzschirme befindet. Es gelingt fast immer die Gelenkspalte zu sehen, auch bei korpulenten Patienten. Wenn man sie nicht zu Gesicht bekommt, stellt sich hinterher fast immer heraus, dass eine Abweichung, eine Ankylose oder etwas Ähnliches, vorliegt.

Wir machen 3 Aufnahmen, weil das Gelenk einige Knickungen zeigt und die Gelenkspalten manchmal ziemlich uneben sind. Zuerst werden die Gelenke unter Durchleuchtung so eingestellt, dass man die Gelenkspalte deutlich sieht; danach werden 2 Aufnahmen bei einer etwas geringeren und einer etwas stärkeren Drehung des Patienten gemacht. Ausserdem wird in jedem Falle eine Übersichtsaufnahme in Rückenlage mit starker Flexion der Oberschenkel gemacht. (Abb. 1.)

Bei *250* Patienten (171 Männer und 79 Frauen) wurde der Winkel gemessen, den die Frontalachse des Beckens mit der Aufnahmeebene (dem Fluoreszenzschirm) macht. Dieser Winkel gibt ein Mass für die Konvergenz des sacroiliakalen Gelenkes nach dorsal hin an. Die Messung geschah folgenderweise: Zwischen Patient und Fluoreszenzschirm wurde ein horizontal gehaltener Zirkel plaziert, dessen einer Schenkel gegen den Fluoreszenzschirm und dessen anderer Schenkel gegen die dorsale Seite des Sacrums gestellt wurde. Der Winkel, den die Schenkel des Zirkels miteinander machten, wurde gemessen. (Abb. 2.)

Zur Deutung der an den 500 Gelenken gewonnenen Masse wurden nur solche Fälle ausgewählt, bei denen die Gelenkspalte auf der Aufnahme optimal frei projiziert worden war. Dies war bei 375 Messungen der Fall. Der Durchschnittswinkel betrug rechts 22.4° (bei Männern 21.8°, bei Frauen 25.1°) und links 19.7° (bei Männern 19.6°, bei Frauen 20.0°). Die individuelle Differenz ist beträchtlich, der grösste Winkel war 37° und der kleinste 3°.

Oft zeigte sich auch eine Asymmetrie zwischen rechts und links. In 89 der 175 Fälle, bei denen die Gelenkspalte auf beiden Seiten ideal projiziert worden war, war die Differenz mehr als 5°, bei 19 Patienten mehr als 10° und bei 8 Patienten mehr als 15°; der Maximalunterschied belief sich auf 19°. Folglich darf man aus diesen Beobachtungen schliessen, dass für halbseitliche Aufnahmen kein bestimmter Winkel angegeben

werden kann, bei dem die sacroiliakale Gelenkspalte völlig frei projiziert wird.

In einer Zeitspanne von 1½ Jahren haben wir 350 Patienten (223 Männer und 117 Frauen) auf diese Weise untersucht. Das Alter schwankte zwischen 18 und 74 Jahren. Bis auf einige Ausnahmen wurden uns alle Patienten von den Beratungsstellen zur Bekämpfung des Rheumatismus in Rotterdam geschickt. Um ein objektives Urteil zu erzielen und den Wert der Röntgenuntersuchung zu prüfen, wurden uns keine klinische Daten mitgeteilt. Erst nach der Beurteilung der Röntgenaufnahmen wurden die Ergebnisse mit der Klinik verglichen. Nach dem Röntgenbilde, das die Übersichtsaufnahme zeigte, können wir drei Gruppen unterscheiden:

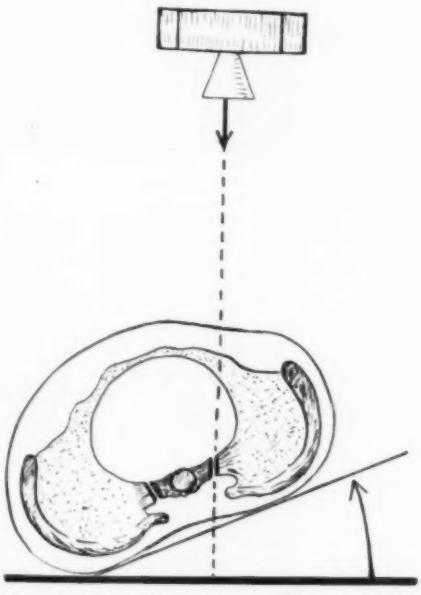


Abb. 2. Einstellung der rechten sacroiliakalen Gelenkes unter Durchleuchtung. Der Winkel ist ein Mass für die Konvergenz dieses Gelenkes nach hinten.

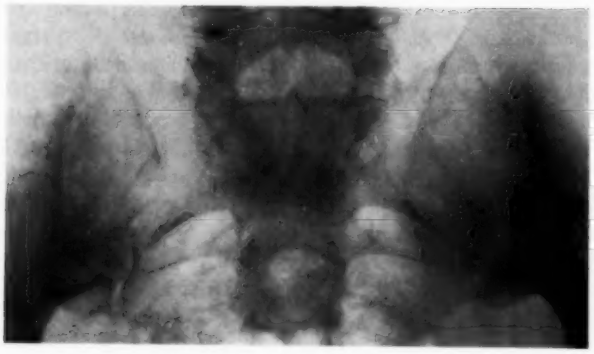
I. *Normales Bild* auf der Übersichtsaufnahme: 124 Fälle. Dabei zeigte sich 121 Mal das Bild auf den gezielten Aufnahmen ebenfalls völlig normal, 2 Mal war es zweifelhaft und 1 Mal pathologisch.

II. *Zweifelhaftes Bild:* 126 Fälle. Bei diesen Kranken war es schwer oder unmöglich, nur an Hand der Übersichtsaufnahme eine Diagnose zu stellen. Die gezielten Aufnahmen zeigten 110 Mal ein normales Bild, 15 Mal ein pathologisches Bild und 1 Mal ein zweifelhaftes Bild. (Abb. 3.)

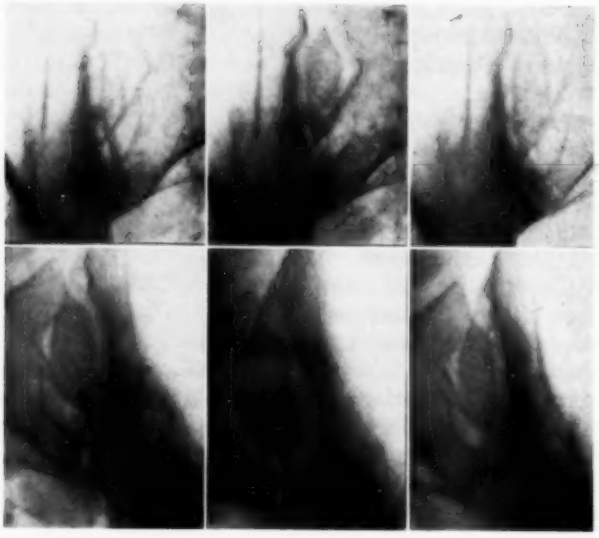
III. *Pathologisches Bild* auf der Übersichtsaufnahme: 100 Fälle. Hiervon zeigten 19 Fälle auf den gezielten Aufnahmen jedoch ein normales Bild; 1 Mal blieb es zweifelhaft, während in 80 Fällen ein unverkennbar pathologisches Bild auch auf den gezielten Aufnahmen wahrgenommen wurde.

Aus diesen Beobachtungen ergibt sich, dass man durch die unter Durchleuchtung angestellten Aufnahmen die Röntgendiagnostik der sakroiliakalen Gelenke erheblich verbessern kann.

Bei Betrachtung der unter Durchleuchtung angestellten Aufnahmen von Patienten mit Bechterewscher Krankheit konnten wir der von KNUTS-



a.



b.

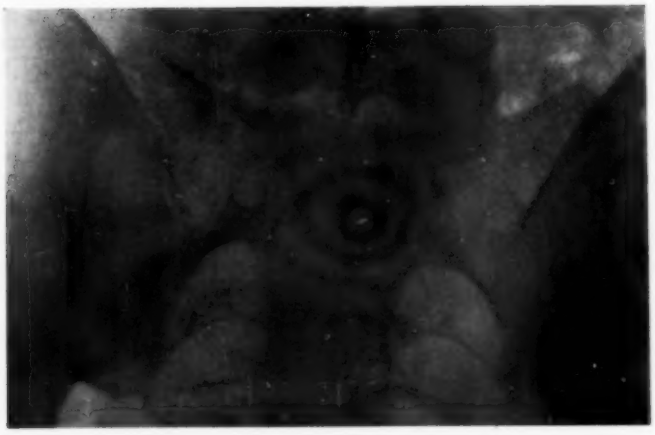
Abb. 3. a. Übersichtsaufnahme: zweifelhaftes Bild.
b. Gezielte Aufnahmen desselben Kranken: Bechterew (Stad. I).

SON gegebenen Beschreibung völlig beipflichten. Die Einteilung in 3 Stadien (I Anfangsstadium, II Destruktionsstadium, III Ankylosestadium) hat sich gut bewährt. Als erste Symptome sahen wir immer eine leichte Sklerosierung der iliakalen Seite des Gelenkes, begleitet von einem unscharfen Umriss der Gelenkfläche und einer geringfügigen Erweiterung der

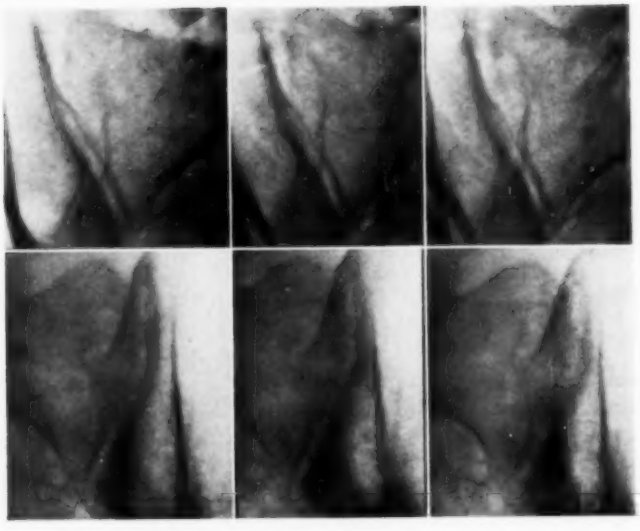
Gelenkspalte. Erst danach werden Veränderungen an der sacralen Gelenkfläche beobachtet. Die Beurteilung der Übersichtsaufnahme ist oft sehr schwierig. Wir sahen häufig Patienten, bei welchen die Übersichtsaufnahmen ein auffallend ähnliches Bild zeigten, während mit gezielten Aufnahmen in dem einen Falle ein völlig normales Bild und im anderen Falle das typische Anfangsstadium einer Bechterewschen Krankheit beobachtet wurde. Die Differentialdiagnose gegen die Osteitis condensans ilii kann jedoch Schwierigkeiten bieten. Bei den 350 Kranken wurde an Hand der Röntgenuntersuchung 87 Mal die Diagnose Bechterewsche Krankheit gestellt und 3 Mal die Diagnose Osteitis condensans ilii; 2 Mal war die Differentialdiagnose gegen diese Krankheit unmöglich, während die Röntgenuntersuchung in 4 Fällen ein zweifelhaftes Resultat ergab. Die klinischen Befunde wurden erst nach Beurteilung der Röntgenuntersuchung erhalten. Es stellte sich heraus, dass 14 Patienten übrigblieben, bei denen die Diagnose Bechterew für sehr wahrscheinlich oder fast sicher gehalten werden durfte, obwohl die Röntgenaufnahmen keine Veränderungen zeigten. Es folgt eine Übersicht der Ergebnisse:

Röntgenuntersuchung	Klinik		Bechterew
	negativ	?	
Negativ			14
Bechterew Stad. I	5	6	23
Bechterew Stad. II	2	—	11
Bechterew Stad. III	3	—	37
Osteitis condensans ilii oder Bechterew?	—	1	1
Osteitis condensans ilii	2	—	1
?	1	1	2

Also zeigte sich, dass es bei 10 Patienten keinen deutlichen klinischen Anknüpfungspunkt gab, so dass die Diagnose Bechterew röntgenologisch gestellt werden musste. Dies entspricht den Beobachtungen von SCOTT, FORESTIER u. a. Es ist möglich, dass man röntgenologisch schon Veränderungen an den sacroiliakalen Gelenken wahrnimmt, wenn es noch kein manifestes klinisches Bild gibt. Mehr fallen die 14 Patienten auf, bei welchen die Diagnose Bechterewsche Krankheit aus klinischen Gründen sehr wahrscheinlich oder fast sicher war, während sich röntgenologisch keine Veränderungen an den sacroiliakalen Gelenken beobachten liessen. Von anderen Autoren wird eine viel niedrigere Zahl angegeben (FORESTIER 2 Mal in 153 Fällen von Bechterewscher Krankheit, KNUTSSON einmal in 147 Fällen, GOLDING kein einziges Mal in 91 Fällen). Es fragt sich jedoch, ob diese Zahl nicht viel höher gewesen wäre, wenn man immer



a.



b.

Abb. 4. a. Übersichtsaufnahme: Beide Gelenke schwer zu beurteilen.
b. Gezielte Aufnahmen desselben Patienten: rechts (oben): normal, links (unten): Bechterew (Stad. I).

genau gezielte Aufnahmen anfertigt hätte. Es ist nicht imaginär, dass Übersichtsaufnahmen der sacroiliakalen Gelenke, welche schwer zu beurteilen waren, in Fällen von Bechterewscher Krankheit für pathologisch

gehalten worden sind, obwohl dieses vielleicht nicht der Fall war. Deshalb sollte man alle diese Kranken in den kommenden Jahren fortlaufend untersuchen. Dasselbe lässt sich auch zu den Fällen sagen, welche röntgenologisch das Bild einer Osteitis condensans ilii zeigen. Bei vier Patienten konnten die Abweichungen ganz sicher nur an einem Gelenk beobachtet werden. Darunter war ein Patient, der schon ein Jahr früher untersucht worden war und damals keine Abweichungen an den sacroiliakalen Gelenken zeigte, aber aus klinischen Gründen stark an eine Bechterewsche Krankheit erinnerte. (Abb. 4.)

Aus dem Obenstehenden glauben wir folgen zu dürfen, dass eine Übersichtsaufnahme der sacroiliakalen Gelenke allein nicht zu einer richtigen röntgenologischen Beurteilung genügt, besonders nicht zum Stellen der Diagnose der Bechterewschen Krankheit. Die halbseitlichen Aufnahmen sind von grosser Wichtigkeit, aber nur wenn die Gelenkspalte völlig frei projiziert wird. Weil es unmöglich ist, einen bestimmten Drehungswinkel für das Becken anzugeben, ist die Einstellung unter Durchleuchtung der geeignete Weg.

ZUSAMMENFASSUNG

Es wird auf die Bedeutung der halbseitlichen Aufnahmen für die Röntgendiagnostik der sacroiliakalen Gelenke, insbesondere für die Stellung der Diagnose der Bechterewschen Krankheit, hingewiesen. Mittels Messungen wird gezeigt, dass sich kein bestimmter Drehungswinkel für das Becken angegeben lässt. Es wird daher empfohlen, die Einstellung dieser Aufnahmen unter Durchleuchtung durchzuführen. Die Ergebnisse der Röntgenuntersuchung von 350 Patienten werden erwähnt. Dabei wurden die Resultate der Röntgenuntersuchung erst nach der Feststellung der Röntgendiagnose mit den klinischen Daten verglichen.

SUMMARY

Attention is drawn to the value of semilateral views in the roentgen diagnosis of the sacro-iliac joints, especially in the diagnosis of Bechterew's disease. Measurements are given to show that there is no fixed angle to which the pelvis should be rotated. The taking of these views under radioscopic control is recommended. The results obtained in 350 patients are reported and were only compared with the clinical findings after the roentgen diagnosis had been established.

RÉSUMÉ

L'auteur insiste sur l'intérêt des radiographies en incidence oblique dans l'examen des articulations sacro-iliaques notamment pour faire le diagnostic de maladie de Bechterew. Les mensurations montrent qu'on ne peut déterminer une fois pour toutes l'angle dont il faut faire tourner le bassin. Il est recommendé d'effectuer la mise au point de ces clichés en radioscopie. L'auteur donne le résultat de cet examen radiologique chez 350 malades. Dans ces cas les résultats de l'examen radiologique n'ont été confrontés avec les données cliniques qu'après l'établissement du diagnostic radiologique.

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FROM THE RADIUM CENTRE IN COPENHAGEN, DENMARK (DIRECTOR: JENS NIELSEN)

LUPUS CARCINOMA; WITH SPECIAL REFERENCE TO THE APPLICABILITY OF RADIOTHERAPY

by

Povl Hjorth

During the past hundred years numerous studies and reports of cases have been published on cancerous changes occurring in lupus vulgaris. This complication, known as lupus carcinoma, has been observed both in lupus vulgaris treated by irradiation with ultraviolet light, roentgen or radium, and in the untreated condition.

The knowledge acquired early in this century of the carcinogenic action of roentgen rays led SEQUEIRA, in 1904, to advise against the exhibition of roentgen therapy in lupus vulgaris; such treatment, in his opinion, would augment the recognized risk of cancer developing. This view was shared by ROWNTREE (1908) whose studies seemed to indicate a rise in the incidence of lupus carcinoma in England following the introduction of roentgen therapy. The same opinion was expressed by HESSE and COENEN who issued a warning on the treatment of lupus vulgaris by roentgen rays which they viewed as an important carcinogenic factor.

As almost all subsequent investigators have taken the same attitude, there exists practically no difference of opinion on this matter. Thus BAUER, in 1949, stated that the treatment of lupus vulgaris by roentgen or radium was not therapy but experimental carcinogenesis.

Only much later was attention directed to the carcinogenic effect of ultraviolet rays. As late as 1921 REYN concluded that the treatment of lupus vulgaris with Finsen light produced no carcinomatous changes and he expected lupus carcinoma to become a rare occurrence after the institution of this therapy. Time has proved him wrong, and a number of studies — all on the carcinogenic action of ultraviolet rays — have since appeared.

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In 1926 ABRIKOSOFF reported the production of basal cell carcinoma-like changes in artificial cicatrices of the skin of rabbits following ultraviolet irradiation. The cicatrices revealed less resistance to light exposure than did the intact surrounding skin. In 1928, FINDLAY succeeded in producing cancer of the skin in albino mice following repeated irradiation with ultraviolet rays.

Only later did research workers use filtrated ultraviolet light and study the effect of different wavelengths. FUNDING, HENRIQUES and REKLING demonstrated, in 1936, that ultraviolet light is carcinogenic up to a wavelength of 3,200 angstroms, and subsequent investigators have been able to verify these first results (BLUM).

For a great number of years, clinical observers have called attention to the importance of sunlight in the development of cutaneous cancer in man, and more recent studies seem to substantiate the correctness of such observations (BLUM, DORN).

In regard to lupus cancer, it appears from the various investigations into this disease that the question of the mechanism of carcinogenesis is undecided. Animal experiments have made it possible to demonstrate the carcinogenic effect of some of the forms of treatment applied in lupus vulgaris, but the processes that take place during the course of the disease in man are extremely complicated, and the experimental results obtained in laboratory animals are not directly applicable to human beings.

The most obvious factors of a complex mechanism are the ones that are most readily observed and, perhaps, unreasonable importance is therefore attached to them. Partly for this reason it remains an open question, when discussing the carcinogenesis of lupus carcinoma, whether local therapy is not given too much prominence and a greater significance than it actually deserves. On the other hand, various clinical observers have so frequently emphasized the traumatizing and supposedly carcinogenic property of local therapy that there is hardly any reason to question its significance in the formation of cancer (WICKMANN, KREINER).

Author's Material

A review was made of the cases of cancer of the skin admitted to the *Radium Centre* between 1931 and 1950, and a group of 27 patients, classified under the diagnosis of lupus carcinoma, was selected for study. Following a closer survey of the case histories, two of the patients had to be excluded as they developed cancer in areas of the skin which, to all appearances, were not involved in the process. Thus, in these instances it was a question of cutaneous cancer occurring in lupus patients, not

of lupus carcinomas. Excluding these two patients the entire group comprised 25 patients with 27 lupus carcinomas.

All these patients developed cancer in definitely changed areas of the skin which were or had been affected with lupus vulgaris at the time when cancer was diagnosed. 23 of the patients were referred from the Department of Dermatology of the Finsen Institute. It is unlikely that this group represents all the cases of lupus carcinoma treated at the Finsen Institute during the said period, since — especially some years back — a number of patients received operative treatment and thus did not pass through the *Radium Centre*, the records of which almost exclusively comprise patients treated by radiation.

As in REYN's series, the histologic examination showed carcinoma planocellulare in the vast majority of cases. Carcinoma basocellulare was diagnosed only in two patients (both females). In two cases there was no histologic examination, and one case revealed no definite microscopic evidence of malignity. All three patients, however, presented typical clinical pictures of cancer.

Distribution according to sex and age. The patients in this study comprised 13 men (with 14 cancers) and 12 women (with 13 cancers).

The author found, as other investigators, that the development of malignancy in lupus vulgaris occurred most frequently in the older age groups. The average age at the time when cancer was diagnosed was 60 in the men and 59 years in the women. (Thus, the average age was only slightly below that reported for autochtonous cancer of the skin in Denmark, which according to JENS NIELSEN is 64.) The youngest patient was aged 37, the oldest 88. 77 % of the patients fell within the age group of 40—70 years.

Table 1 shows the distribution of the author's series in the various decades of life.

Table 1

Age	M.	F.
30—40	1	1
40—50	2	2
50—60	4	3
60—70	5	5
70—80	2	1
80—90	0	1

Latent period before the development of cancer. The duration of the lupous process, or the latent period before the development of cancer, varied considerably. The shortest latent period observed was 13 years, the longest 70.

The average latent period was 39 years in the men and 40 in the women. Most investigators report this period as being about 30 years.

It was a peculiar phenomenon that the latent period was shorter (37 years) in the patients who received light therapy alone than in those who, in addition to light therapy, were given roentgen or radium treatment. In the latter group the latent period was 43 years. This may be accounted for by the fact that these patients received only moderate doses of roentgen therapy, since otherwise the latent period might have been expected to have been appreciably shortened. According to LACASSAGNE the average latent period before the development of roentgen carcinoma following therapeutic irradiation is 14 years — computed from the data reported in the literature.

Situation. All the lupus cancers discussed here developed in areas of the skin which had been habitually exposed to light, and there was no instance of cancer originating in mucous membranes, although in 17 of the 25 patients there was lupous involvement of the mucous membrane, frequently attended by severe changes in the form of persisting ulceration and the formation of crusts. In particular the mucous membrane of the nose was affected.

The treatment of the lupous affections of the mucous membranes was, on the whole, less intensive than that applied in lupus vulgaris of the skin. In some instances the vestibule of the nose was irradiated with Finsen light (prism light), sometimes in combination with cauterization; turbinectomy was occasionally performed in the presence of pronounced hypertrophy. Two of the patients were given roentgen therapy for lupous involvement of mucous membranes, one on the inside of the lips and the hard palate, respectively.

It is generally accepted that lupus carcinoma is a rare occurrence in mucosal affections. Previous investigators have, however, reported cases of such a situation (ASHIHARA, SILBERSTEIN). In a review in 1946, SANDER-LARSEN found the mucous membrane to be the primary site of lupus carcinoma in 3 out of 32 cases. REYN's series included no cancers involving the mucous membrane.

Various factors would appear to account for the rare tendency of lupus cancer to develop in mucosal affections. Firstly, mucous membrane, of course, differs anatomically from skin — for which reason alone it holds an exceptional position. Secondly, because of its situation, mucous membrane is less subject than the skin to repeated trauma — being protected from exposure to sunlight and the more common influences of wind and weather. Thirdly, it is less accessible to local therapy.

10 of the cancers developed at the original site of lupus vulgaris, which in all cases corresponded to the area that had been exposed to

local therapy for the greatest length of time. There were numerous histories of recurrent chronic ulceration during the course of treatment preceding the development of cancer, and 19 out of 27 cancers arose at the site of such changes. Previous investigators held that the presence of ulceration had no influence on the development of cancer. WICKMANN and REYN did not believe that the proliferating processes of lupus vulgaris constituted a disposition to the development of cancer. It is the author's view, however, that it was hardly accidental that such a high proportion of the cancers in this investigation arose at the identical site of previously persisting ulceration and proliferation. Only 7 cases presented smooth cicatrices with no indication of florid lupus vulgaris at the time when cancer was diagnosed. Thus, even though smooth cicatrices do not, as suggested by REYN, offer a guarantee against the development of cancer, it would appear to occur most frequently in cicatrices, which have been the site of florid lupus vulgaris with ulceration and proliferation.

It was not possible, from the present investigation, to decide — with any degree of certainty — the importance of roentgen therapy in the development of cancer. A study of the case records yielded no definite information as to the doses given (the treatments dated back many years). However, the data available concerning the latent period in relationship to the formation of cancer would suggest that only small quantities of roentgen therapy were administered and that the patients received mainly ultraviolet irradiation in the treatment of the lupus vulgaris. Another indication pointing in this direction was the appearance of the cicatrices of the patients treated by roentgen which closely resembled those resulting from Finsen light therapy. Thus, there was apparently no single instance of pure roentgen cancer.

It will be interesting to learn something of the results obtained in cases of lupus vulgaris treated only with ultranol. It is possible that its use will reveal cancer prophylactic properties, since it will probably render superfluous the constant damaging effect of local therapy which seems to be a decidedly important factor in the development of cancer.

Treatment and Prognosis

There has been general agreement among previous investigators of lupus carcinoma that this variety of cancer is a thankless object of treatment and that radiotherapy offers poor prospects of cure.

As a result of his studies 1921, REYN recommended local excision in healthy tissue as the best method of approach and regarded this form of therapy as infinitely superior to radiotherapy which he thought would almost invariably yield disappointing results.

Further contributions toward the solution of the question of the applicability of radiotherapy in lupus carcinoma were made in 1935 by MÜNDELEIN and in 1937 by PLACZEK. Their reports, however, did not clearly define the lines on which treatment was carried out. As a rule, small cancers were removed by excision. The inoperable cases were treated with roentgen, but no details of treatment were given apart from the total doses administered. No mention was made of the degree of fractionation which must be deemed an essential factor in cases such as these of cancer involving cicatricial tissue. The investigators gave the same prognosis to all their cases, but on close examination these appear to be as heterogeneous as those now reported. There were instances of small, superficial, well-defined cancers which responded satisfactorily to the form of therapy employed (as a rule, excision) and of large, infiltrating, rapidly growing cancers producing considerable loss of substance and, frequently, cavities due to necrosis. These latter cancers failed to heal in response to radiotherapy, either administered alone or in combination with mutilating, major, surgical intervention.

A recurring feature of all published reviews is the relatively infrequent occurrence of metastatic regional glands in lupus carcinoma. (Incidentally, ordinary cancer of the facial skin but rarely metastasizes.) Furthermore, metastases in distant parts are very rarely observed in this disease. In 16 out of 122 patients ASHIHARA found metastatic involvement of regional glands. SILBERSTEIN reported 7 cases of such involvement in 111 patients. In PLACZEK's series of 28 patients, 2 had glandular metastases, and in the present group of 27 lupus carcinomas there were 4 instances of metastatic involvement of regional glands.

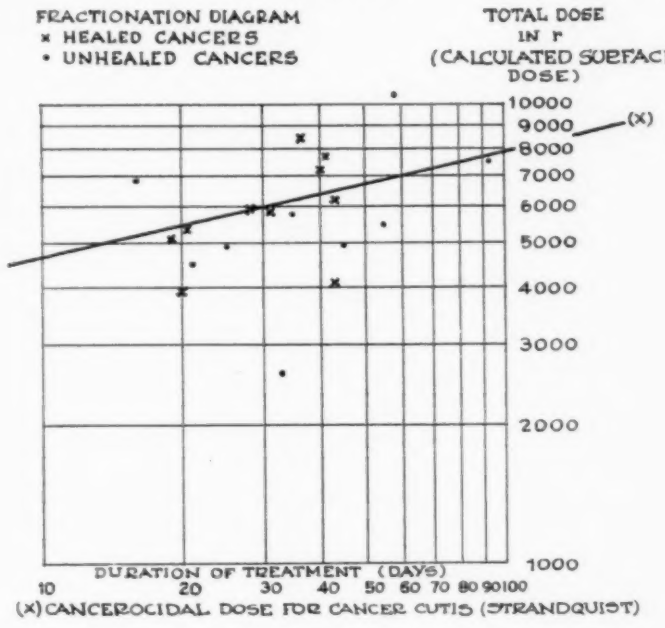
The publications of the aforementioned authors contained no information as to whether or not their patients presented evidence of florid lupus vulgaris during the course of treatment. Florid lupus vulgaris was present during the course of treatment of 20 of the 27 cancers in this study.

An attempt was made to classify the cancers according to size (superficial extension), depth, possible terebrating invasion of subjacent bone or cartilage, and metastases to regional lymph nodes. Later, mention will be made of the decisive influence of these factors and the recurrence of lupus vulgaris in the cicatrix on the radiocurability of the patients.

Radiotherapy. Of the 25 cases in this study subjected to radiotherapy, 19 received roentgen and 6 radium treatment. In 5 instances radium was administered by needle implants in doses varying from 90 to 1,200 mg hours. In one case a radium mould was used, and radium was administered in fractional doses up to a total of 1,440 mg hours.

The 19 cases treated by roentgen received highly fractionated, individually adjusted doses with close observation of reactions at brief intervals. It was thought that this procedure would enable administration of a cancerocidal dose causing the least possible damage to the surrounding tissues. The total dose in most instances thus corresponded to the dose which STRANDQUIST considered adequate for the destruction of skin cancer. The following diagram shows the calculated individual surface doses, entered on STRANDQUIST's chart. It will appear, however, that there was no decided difference in the doses administered to the successfully and the unsuccessfully treated cases.

Table 2



The principles on which roentgen therapy was administered were as follows:

9 cases received 180 kV, 4—6 mA, Thoræus filter, at 40—50 cm target—skin distance (H. V. L. 1.75 mm Cu). Three other cases received 165 kV, 4 mA, Thoræus filter, 50 cm distance (H. V. L. 0.90 mm Cu) and 4 cases 100 kV, 6 mA, 3 mm Al, 40 cm (H. V. L. 0.3 mm Cu). Short distance roentgen therapy was given in 3 instances (60 kV, 4 mA, 0.1 mm Cu, 7.5 cm, H. V. L. 2.2 mm Al).

The size of the radiation fields varied and was frequently reduced after a period of treatment. For the small cancers only one field was used, aimed directly at the tumour; for the more extensive growths two or three fields were used with tangential irradiation; towards the end of treatment the fields were usually reduced to one, aimed directly at the tumour. The average size of the radiation fields was 50 cm², the smallest being 7 cm², the largest 80 cm².

Illustrative Case Reports

Case 1. Male, aged 68. Lupus vulgaris of external aspect of nose began when the patient was 18. At the onset he was treated with mercury ointment and scraping. The lesion subsequently remained healed until 6 months prior to admission to the Finsen Institute (Sept. 1903), when he was found to have a scar-like lesion, with ulceration of right cheek; the nose was however highly defective.

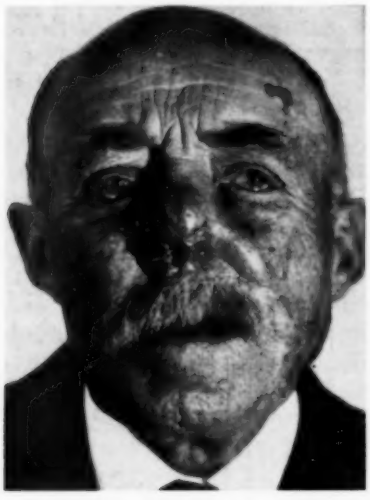


Fig. 1 a.

Fig. 1 b.

Courses of Finsen light were given yearly up to 1917. Roentgen was administered in 1910, 1911, 1913, and 1914 — 8 exposures to upper lip and nose, due to ulceration of both alae nasi. (Dosage not accurately known.) Complete healing since 1917.

At the *Radium Centre*, Nov. 1933, the patient stated that nasal ulcerations of rather rapid growth had developed during the preceding two or three months.

Nov. 1933 (Fig. 1 a): clinical examination revealed mainly soft cicatrices of the cheeks, resulting from the previous lupous affection. On the left cheek were two circular hyperkeratoses, one about 2 cm, the other about 1 cm in diameter.

The lower part of the nose was destroyed; the nostrils were surrounded by a tumourous ulceration, measuring 4.5 × 3.5 cm. The edges protruded, were highly necrotic in parts and hard to the touch. The nostrils were almost completely blocked by tumour

tissue and there was extension on both sides for about 2 cm into the nasal cavity. The growth adhered firmly to the remainder of the cartilage, possibly also to the maxilla.

In the right carotid triangle a small, fixed gland, situated close to the blood vessels was noted. No visible changes of the skin.

Microscopic diagnosis: carcinoma planocellulare. Roentgen therapy was given in fractional doses. Three fields were irradiated, one aimed directly at the nose and one to either side. Dosage: 5,675 r in air/40 days. Radiation field 48 cm², 180 kV, 4 mA, 68 cm, Thoræus filter. Subsequent examination revealed complete regression of exterior tumour but residual growth in nasal cavity.

Febr. 1934: electrocoagulation of nasal cancer. Resection of both alae and philtrum. Subsequent healing. At the follow-up examinations there was no evidence of recurrence and no development of radionecrosis.

Follow-up April 1941 (Fig. 1 b) revealed an overall smooth cicatrix with no indication of recurrence. No involvement of regional glands.

Fig. 2 a.

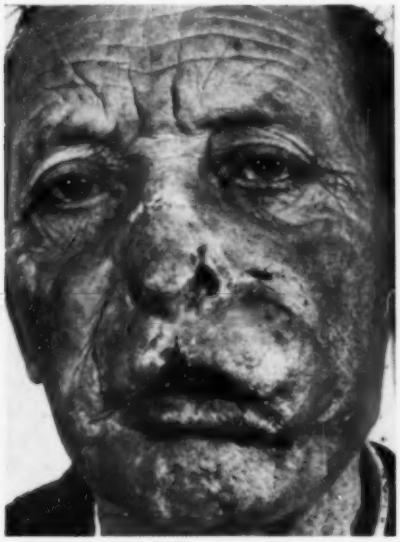


Fig. 2 b

In May 1950 the patient died from intercurrent disease (morbus cordis) showing no sign of recurrence of the lupus cancer. He had then been symptom-free for 17 years.

Case 2. Male, aged 58. Lupus vulgaris from the age of 18 years. Finsen light was given at the Finsen Institute in 1902—1911 and in 1923. The lesion treated was localized to the right palpebra superior and the right cheek. The patient also received roentgen treatment to nose — 6 exposures in 1908, 1909 and 1910, and one exposure in 1923. (Dosage not accurately known.)

There was then complete healing, and no further form of treatment was administered.

Dec. 1940 the patient was referred to the *Radium Centre* for treatment of a crust-covered ulceration of left ala nasi of about 6 months' duration.

Dec. 1940 (Fig. 2 a) the skin had healed nicely after the lupus vulgaris; the left ala nasi, however, was somewhat defective. On the left ala nasi there was a crust-covered ulceration, about 1 cm in diameter. No involvement of regional glands.

Microscopic diagnosis: carcinoma planocellulare. The patient was given short distance roentgen therapy: one field measuring 7 cm², aimed directly at the tumour. Total dose 5,600 r. in air/31 days. Complete regression of tumour and no evidence of radionecrosis.

(Jan. 1947 the patient again presented himself at the *Radium Centre* and was given fractional roentgen therapy for cancer of the prolabium; Jan. 1950 a recurrence was treated by total extirpation followed by transplantation.)

Febr. 1950 (Fig. 2 b) the cicatrix resulting from the previously treated lupus cancer was completely soft.

Fig. 3 a. Fig. 3 b.

Case 3. Male, aged 52. Lupus vulgaris began in early childhood. Courses of Finsen light were given yearly at the Finsen Institute from 1903 to 1912, and again in 1927 for ulceration of right angulus oris and right submental region. The patient also received roentgen therapy in 1908, 1909, and 1912 — four exposures to right side of upper lip, both externally and internally. (Dosage not accurately known.)

No further treatment given until 1939 when Finsen light therapy was resumed. At that time there was an extensive cicatricial formation all over the front part of the neck and under the chin. Ulceration in latter situation. No involvement of upper lip. Microscopic examination of specimen removed from under chin revealed hyperkeratosis. No sign of malignancy. The lesion healed in response to Finsen light, and the treatment was discontinued.

Aug. 1941 (Fig. 3 a) the patient was referred to the *Radium Centre*. During the preceding three months a wart-like affection had developed on the prolabium of the right upper half of the lip, on the skin border; it grew rather rapidly and ulceration developed.

Clinical examination revealed smooth, movable cicatrices of right cheek, chin, and both submaxillary and submental regions. A bowl-shaped area of ulceration, measuring 3.3×1.6 cm, occupied the lateral half of the prolabium of the right upper lip, reaching as far as the angulus oris, involving part of the cheek and extending forwards about 0.5 cm into the right side of the lower lip. There was pronounced protuberance of the edges and infiltration extending backwards for about 1 cm on the inside of the right cheek. No indication of lupus vulgaris.

Microscopic diagnosis: carcinoma planocellulare. Aug.—Sept. 1941 roentgen was given in fractional doses totalling 7,260 r in air/36 days, 180 kV, 4 mA, Thoræus filter, 50 cm in one field, measuring 15 cm^2, aimed directly at the tumour. Complete healing in response to treatment.

Follow-up examination May 1942 (Fig. 3 b) revealed no recurrence and no radionecrosis. The cicatrix resulting from light therapy extended as far as the right angulus oris and the site of the original cancer did not differ essentially from the remainder of the cicatrix.

Subsequent follow-up examinations revealed the same conditions. The patient has remained symptom-free for 10 years.

Results of Treatment

The cases in which there was a follow-up period of at least 5 years comprised 21 carcinomas (in 20 patients). 15 of these received roentgen treatment, 6 were treated by radium.

All the cases treated by radium remained symptom-free for at least 5 years. One case developed a recurrence 7 years after treatment.

Of the 15 cases treated by roentgen, 6 remained symptom-free for at least 5 years — one patient died without recurrence of symptoms 9 months after treatment was discontinued. One patient became symptom-free, but had a recurrence 1 year later (died of heart failure). 7 cases failed to become symptom-free and died of lupus cancer 2, 2, 4, 5 and 7 months, $2^1/_4$ and 3 years respectively after treatment was discontinued. — All the cases responding favourably to treatment remained healed (as mentioned there were only two instances of recurrence) and did not develop radionecrosis.

A direct comparison with previously reported results of treatment is not possible because of varying or unknown means of selection and differing methods of therapy. With these reservations the results of certain previous investigations will be mentioned. In MÜNDELEIN's series of 83 patients, 3 were free from symptoms for 5 years or more; in 6 out of 16 patients REISNER found no recurrence of symptoms over a similar period; PLACZEK reported no evidence of recurrence in 4 out of 28 patients, and in SANDER-LARSEN's group of 32 patients, 3 remained symptom-free for at least 5 years.

The cancers treated by radium were of small size and excepting in the case treated by radium mould were all superficial and well-defined and presented no major therapeutic problems. In the case of the two largest growths excision was carried out prior to radium therapy; the remaining four were treated by radium needle implants alone.

The more extensive cancers were assigned to roentgen therapy, and as previously mentioned (cf. Table 2), the successfully treated cases appeared to have received essentially the same doses of roentgen as those in which no healing took place. (In one case excision of the residual tumour was performed.)

On the other hand there was a noticeable difference in the incidence of the aforementioned unfavourable factors which occurred much more frequently in the unhealed group (Table 3).

Table 3

Frequency of Unfavourable Conditions in Entire Group Irradiated.

	Treated by roentgen		Treated by radium	
	Healed	Unhealed	Healed	Unhealed
No. of cases	10	9	6	0
Infiltration of soft parts	3 (30 %)	7 (78 %)	1 (16 %)	—
Invasion of bone or cartilage	2 (20 %)	4 (44 %)	0	—
Metastases to regional glands	0	4 (44 %)	0	—
Extension exceeding 3 × 4 cm	2 (20 %)	7 (78 %)	0	—
Florid lupus vulgaris of cicatrix	4 (40 %)	7 (78 %)	0	—

It would thus appear that these unfavourable factors had a decidedly adverse influence on the results of treatment, and based on their presence lupus cancers may be divided into groups of varying prognosis and radiocurability.

Conclusion

The mechanism of the carcinogenesis of lupus carcinoma has not been elucidated. There are apparently many factors which contribute to the production of cancer and, in an attempt to offer an explanation, it would be equally wrong to focus one's attention one-sidedly on the effect of local therapy given during the course of lupus vulgaris as to disregard it completely. Several previous authors regarded roentgen therapy as the factor largely responsible for the formation of cancer in lupus vulgaris. It is presumed, however, that roentgen therapy played a minor rôle in the treatment of the patients under discussion who received mainly Finsen light. Evidence has been presented of the carcinogenic property of roentgen rays, and there was nothing in the present study to disprove the view that a considerable risk may be involved in the use of roentgen therapy for lupus vulgaris. Judging from the ap-

pearance of the cicatrices and the available data concerning the latent period of the development of cancer, it would appear that the patients under review received only moderate doses of roentgen therapy. Thus, the cicatrices of the group irradiated by roentgen or radium prior to the onset of cancer were similar in appearance to those observed in the group treated by Finsen light alone; since there was no single instance of definite roentgen cicatricial skin changes in the former group, the carcinomata in both groups responded equally well to the subsequent exhibition of radiotherapy and revealed no demonstrable difference in prospects of cure. Thus, the cured cases never developed radionecrosis.

Based on the theory that lupus carcinoma, by reason of its situation, would appear as ordinary cancer of the skin, to be a form of malignancy caused by exposure to light, the continuation of actinotherapy over a period of years is not perhaps quite so insignificant as generally assumed. Constantly repeated light therapy constitutes sustained trauma of the skin and, as lupus cancer is usually confined to those areas which are exposed to solar rays, lupous patients are between two lines of fires when exposed to the carcinogenic wavelengths of both solar and artificial rays. Apparently the cicatricial changes produced by the lupous process result in a lowered resistance to the (carcinogenic) influences of both radiation and other forms of local therapy.

In regard to the administration of roentgen or radium therapy in lupus cancer, the present study seemed to justify the conclusion that in spite of the poorly vascularized tissue, such treatment is not devoid of promise and may be given in cancerocidal doses without development of radionecrosis. The prospects of cure are apparently lowered by the presence of the following unfavourable conditions: Extension over a surface of at least 3×4 cm; invasion of bone or cartilage; terebrating growth and metastases to regional lymph nodes. Florid lupus vulgaris of the cicatrix also appears to be an indication for poor prognosis, since it occurred most frequently in the cases responding unfavourably to radiotherapy.

On the basis of the aforementioned factors, lupus cancers may be divided into groups of greatly varying prognosis and radiocurability.

SUMMARY

Previous works on lupus carcinoma and experimental studies of the carcinogenic action of ultraviolet rays are reviewed. The present study comprised 27 cases of lupus carcinoma, treated at the Radium Centre in Copenhagen between 1931 and 1950. It was found that radiotherapy may be administered successfully in lupus carcinoma without the development of radionecrosis.

Unfavourable circumstances producing a poor prognosis were: 1) extension of the process over a surface exceeding 3×4 cm, 2) invasion of bone or cartilage, 3) terebrating

growth, 4) metastatic involvement of regional glands and 5) florid lupus vulgaris of the cicatrix.

ZUSAMMENFASSUNG

Frühere Arbeiten über Lupuskarzinom und experimentelle Studien über die karzinogene Wirkung der ultravioletten Strahlung werden durchgesehen. In dieser Arbeit werden 27 Fälle von Lupuskarzinom geschildert, die während der Jahre 1931—1950 im Radiumzentrum in Kopenhagen behandelt worden sind. Man fand, dass Radiotherapie mit Erfolg beim Lupuscarcinom benutzt werden kann ohne dass eine Radionekrose entsteht.

Ungünstige Verhältnisse mit schlechter Prognose waren: 1) Ausbreitung des Prozesses über eine Fläche von mehr als 3 × 4 cm. 2) Einwachsen in Knochen oder Knorpel. 3) Infiltratives Wachstum. 4) Metastasen in den regionären Lymphdrüsen und 5) floride Lupus vulgarisveränderungen in der Narbe.

RÉSUMÉ

L'auteur passe en revue les travaux antérieurs sur le cancer sur lupus et les études expérimentales sur l'action cancérigène des rayons ultra-violets. La présente étude comprend 27 cas de cancer sur lupus traités au Centre du radium de Copenhague de 1931 à 1950. La radiothérapie s'est montrée efficace dans le cancer sur lupus sans donner lieu à radionécrose.

Les facteurs de mauvais pronostic étaient: 1) l'extension du processus sur une surface dépassant 3 × 4 cm; 2) l'invasion de l'os ou du cartilage; 3) une tumeur térébrante; 4) l'envahissement métastatique de ganglions régionaux; 5) et un lupus vulgaire floride de la cicatrice.

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BOOK REVIEWS

TRATTATO DI STRATIGRAFIA. By A. Vallebona. 347 pages, 290 illustrations. Fr. Vallardi, Milano 1952.

In this textbook on laminagraphy by Vallebona as principal author and thirteen collaborators, the history of laminagraphy is carefully surveyed and the outstanding contributions of the radiologic school of Genoa in this field are pointed out. The terms planigraphy and tomography are criticized. The method gives a representation of a stratum or lamina rather than of a plane or of a section. The terms stratigraphy or laminagraphy are therefore to be preferred. The purpose and advantage of the 'usual laminagraphy in a—p and lateral projections is the avoidance of the superimposition and cancellation of shadows which, in certain cases, are so disturbing in conventional roentgenograms. On the other hand the more recent 'axial transverse laminagraphy' permits of axial films of parts of the body (chest, abdomen) not suited for examination axially by the usual roentgenological technique. Axial transverse laminagraphy has solved the problem of three dimensional roentgenography. The fundamentals of the theory of laminagraphy are reported clearly and thoroughly. A chapter of the book deals with laminagraphic apparatus.

A large part of the work is dedicated to the chest. Vallebona emphasizes the importance of a good technical quality of the laminagrams. Fine focus tubes, long focus-film distance and short exposure times must be used. In the study of pulmonary tuberculosis laminagraphy may afford considerable information. Tuberculous cavities not to be seen in conventional roentgenograms are sometimes demonstrated by laminagraphy. This method is stated to be also of assistance in the study of pulmonary lesions other than tuberculosis. Although convinced of the usefulness of laminagraphy in examinations of the lungs the reviewer considers that frequently a pulmonary lesion is 'more clearly seen' in laminagrams than in conventional roentgenograms without the former however, necessarily giving 'more information'. Axial transverse laminagraphy appears to promise a contribution to the study of the mediastinum. By its use the diameters of the heart also may be directly ascertained; this should greatly increase the precision of the determination of the volume of the heart. The differential diagnosis between aortic aneurysms and other mediastinal space-occupying lesions may sometimes be elucidated by axial transverse laminagraphy. The same method may aid in diagnosing hypertrophy of the thymus which sometimes simulates increase of the cardiovascular image. Axial transverse laminagraphy has also been used in the study of the mediastinum after the performance of anterior or posterior pneumomediastinum.

Laminagraphy, when combined with retroperitoneal insufflation, has been shown recently to be a useful method in the investigation of the abdomen. It is possible to obtain strikingly clear visualization of the pancreas by axial transverse laminagraphy after the performance of retroperitoneal, together with gastric, insufflation. Laminagraphy is stated to be useful in the study of the skull and of the ventricular system of the brain (after performance of encephalo- or ventriculography). Truly demonstrative cases are however, in the reviewer's opinion, not included in the book. A chapter of the volume deals with laminagraphy of bones.

The work presents an excellent survey of the subject and it is to be hoped that it will be published in English.

Giovanni Di Chiro.

CONTRIBUTIONS TO THE THEORY AND TECHNIQUE OF QUANTITATIVE AUTORADIOGRAPHY WITH P^{32} WITH SPECIAL REFERENCE TO THE GRANULOSA TISSUE OF THE GRAAFIAN FOLLICLES IN THE RABBIT. By Erik Odeblad. 123 pp, 54 diagrams and illustrations. Acta radiol. Suppl. 93. Stockholm 1952. Swed. Kr. 20: —.

The monograph describes attempts to measure by quantitative autoradiography the amount of radioactive phosphorus (P^{32}) in the ovarian granulosa tissue of the rabbit at different intervals of time after the intravenous injection of P^{32} as orthophosphate. In order that such measurements could be carried out, the theory of the subject and the technique had to be elaborated in detail.

The histologic method used was found to cause a certain degree of shrinkage and partial dissolution of the radioactive compounds present in the ovaries, and this complicated the biologic interpretation. With 0.5 per cent trichloracetic acid in 6 per cent formalin as a fixative, considerable amounts of what are known as acid-soluble and lipid-soluble phosphorus in addition to the nucleic acids appear to have been retained in the sections.

The photographic fundamentals of autoradiography were investigated with a view to obtaining controlled exposure and development and in turn, reproducible results with a defined mean error in photographic density.

A recording densitometer employing a new electronic tube coupling, was constructed; this enabled an a. c. modulation of the light signal to be obtained and ensured proper amplification and recording. The circuit and incorporated photometer are described in detail.

The physical principles of the autoradiographic exposure with special reference to the geometric relationships between emulsion and section were investigated. The application of a fundamental equation permitted calculations from the photometer records of the amounts of P^{32} in the granulosa tissue, of the Graafian follicles in the rabbit.

It was found that after injection in the rabbit of 1 mC of P^{32} per kg body weight, 24—44 atoms of P^{32} per 1,000 μ^3 were present in the sections of the normal granulosa and 16—20 atoms of P^{32} per 1,000 μ^3 of the atretic granulosa ($^1/_2$—48 hours after injection).

The depression of the nucleic acid resynthesis by the beta radiation from P^{32} complicated the interpretation of the results. The combined use in the future of sulfhydryls and the new isotope P^{33} so that irradiation damage may be reduced and resolution and density increased, is discussed. *Autoreview.*

BOOKS RECEIVED

We acknowledge with thanks under this heading books received for review, which we trust will be regarded as a sufficient mark of appreciation of the courtesy of the sender. The reviews of selected items will appear as soon as opportunity affords.

GRUNDLAGEN DER THERAPEUTISCHEN STRAHLENWIRKUNG. Von Herman Holthusen. Verlag Conrad Kloss, Hamburg 1.

ANGIOCARDIOGRAPHY AS A DIAGNOSTIC AID IN CONGENITAL HEART DISEASE. By J. W. C. de Groot. Publisher Keesing, Amsterdam.

ROENTGEN EXAMINATIONS IN ACUTE ABDOMINAL DISEASES. By J. Frimann-Dahl. Charles C. Thomas, Publisher, Springfield, Ill.

THE DIAGNOSIS OF GASTRIC MUCOSAL PROLAPSE WITH EMPHASIS ON THE RADIOLOGICAL FEATURES. By A. D. Keet Jr. Diss. Amsterdam University.

DIE ZEREBRALE ANGIOGRAPHIE. Von H. Krayenbühl & H. R. Richter. Georg Thieme Verlag, Stuttgart.

SELECTED PAPERS FROM THE ROYAL CANCER HOSPITAL AND THE CHESTER BEATTY RESEARCH INSTITUTE, London. Vol. 6.

RESULTS OF TREATMENT OF CANCER IN SASKATCHEWAN 1932—44 (inclusive). By T. A. Watson. Edited by Saskatchewan Cancer Commission.

7th International Congress of Radiology 1953

Oster Voldgate 10, Copenhagen K, Denmark
Cable address: Radiology, Copenhagen

The *Preliminary Programme* was despatched in June, 1952, to 12,000 radiologists throughout the world. Anyone failing to receive a copy should write to the Congress Office, stating whether they would prefer the English, French, German, or Spanish version.

It would be greatly appreciated if potential members would *enrol as early as possible* so that their applications may be dealt with promptly. Too many enrolments on and around the closing date (January 1st, 1953) will cause delay.

Applications for *hotel accommodation* should be sent on Form B to the Congress Office at the time of enrolment. First class hotel accommodation will be limited but priority will for the most part be given to those who apply early.

Those *proffering papers* are requested to enclose *three* copies of their abstracts, which may be submitted in either English, French, or German (one language only).

Members bringing *cars* are advised to indicate this on enrolment.

SCIENTIFIC PROGRAMME

General Meetings

1. Potential developments in radiology
2. Contrast media in diagnosis and risks associated therewith
3. Radio-resistance
4. Protection against ionising radiations
5. Uniformity in therapeutic cancer statistics

Section Symposia

Diagnosis

1. Angiocardiography
2. Tumours of the lung
3. Osteochondrosis of the spine
4. Tomography

Biology

1. Chemotherapy of cancer
2. Isotopes in biology
3. Intra-cellular radiation action
4. Pathogenesis of leucaemia

Technology

1. Diagnosis with high voltage rays
2. The photo-electric timing of roentgen exposures
3. Rapid serial angiography
4. High voltage particle accelerators

Therapy

1. Radioactive isotopes in medial therapy
2. Present status of radiotherapy in benign diseases
3. The radiation syndrome
4. Cancer of the cervix uteri

Physics

1. Recent advances in the diagnostic applications of the fluorescent screen
2. Moving field therapy
3. Integral dose

FLEMMING NØRGAARD
Secretary-General.

September, 1952.